

When Governments Should Help Lamé Dogs

THE financial collapse of Rolls-Royce Limited a year ago has evidently left a deep scar on British political and industrial life, and there is very little prospect that this will quickly disappear. The British Government's account of the sequence of events leading up to the debacle, published last week as a white paper (Cmnd 4860, HMSO, £0.21), does much less than might have been expected to throw light on the reasons why a great public company such as Rolls-Royce was allowed to get into such a mess. The white paper does, it is true, make it clear that by the summer of 1970 the Industrial Reorganization Corporation (as it used to be) had asked some sceptical questions about the strength of Rolls-Royce.

Why were the profit forecasts always optimistic? Was it really sensible for the company to have regarded much of its expenditure on research and development as a capital asset? For organizations where research and development are bound to be a large proportion of the cost of selling manufactured products, and where the time scale for development is long, it may be proper to capitalize the cost of research and development in this way, yet there should have been more anxious questions much sooner about the scale on which Rolls-Royce had been operating in this way in the second half of the 1960s turning paper losses into paper profits. The summary of the IRC report, now published in the white paper, does not, however, support the contention that the British Government would have known much sooner of the shaky condition of the aircraft company if only it had listened to the corporation—it is just as fair to say that if the IRC had smelt a rat in the summer of 1970, it should have set in train a proper investigation of the company's affairs rather than arranging for a further loan of £20 million.

In the second half of 1970, it is with hindsight clear that Rolls-Royce was financially quite out of control, chiefly because of the strains created by the development of the RB-211 engine. The development cost, originally set at £60 million, had already doubled by the time the British Government agreed, in November 1970, to persuade a consortium of banks to lend a further £18 million and to put up £42 million on its own account. But by January 1971, when the company eventually became bankrupt, it is clear from the white paper that nobody was in a position to make an accurate estimate of the cost of carrying through the development of the engine, although it was by then apparent that extra funds would be necessary and that technical success in the development of the engine would not allow the company to make a profit on its products.

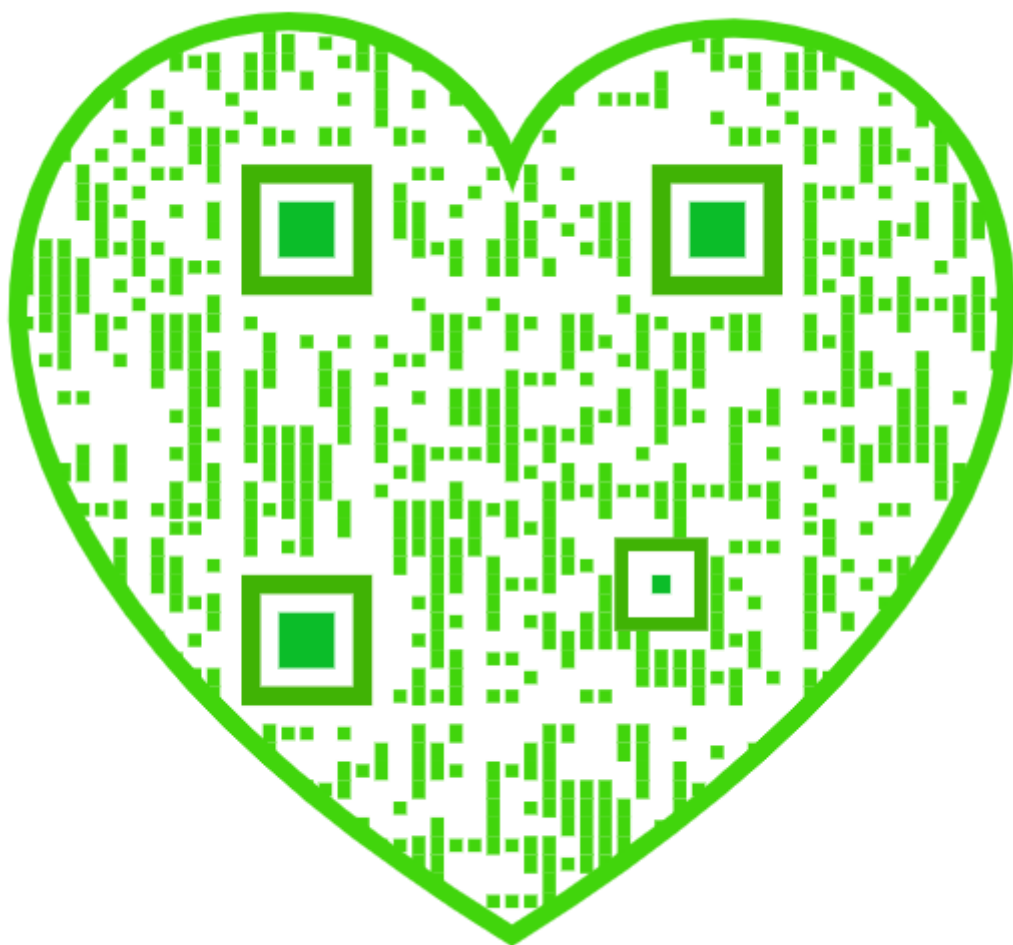
For all practical purposes, at that point in time, the capital assets supposedly created by past spending on research and development were literally worthless—Rolls-Royce would no doubt have wished for nothing better than to be released without penalty from its contract with Lockheed. In all the circumstances, it is a

piece of luck that the technologically advanced part of the company still exists as a kind of subsidiary of the British Government. Last week's white paper finishes with the sanctimonious hope that the foundations have somehow been preserved for a vigorous aircraft engine manufacturing industry in Britain, but readers of the document will quite naturally ask whether the right lessons have been learned.

First of all, it is important that the government should have a better understanding of the circumstances in which technologically advanced products such as aircraft engines can be developed. However much ministers of state may huff and puff, it is impossible to calculate accurately in advance the cost of research and development. The same is true, of course, in industries less technically adventurous than that of aircraft manufacturing—what design engineer will be willing to go to the stake for his estimate of the cost of developing, say, an improved can opener? In high technology, however, where the cost of research and development is a larger proportion of the likely revenue, errors in estimates of development cost are more serious in their effects. One consequence of the Rolls-Royce bankruptcy is that it will now be more difficult than ever to persuade British engineering companies to break new ground in ways like this.

One of the lessons for the government is that some means must be found of supporting major innovations when there are good reasons to suppose that in the long run these may serve the national interest. Especially in telecommunications and transport, there are good reasons why the pace of innovation in Britain should be usefully increased. Nobody asks that the government should cease to be discriminating about the projects that it backs. Chauvinistic ambitions to replicate in Britain technical innovations which have been successful elsewhere are to be deplored and it is only right and proper that government backing for industrial innovation should in due course be repayable by means of levies and royalties; yet in the innocent belief that British industry will learn to stand on its own feet if it is denied financial help for innovation, the British Government is now diligently working towards a policy of studied indifference. Like its predecessor, the present government is increasingly letting the industrial research associations sink or swim. The Industrial Research Development Corporation languishes. It is something of a paradox that all this should happen at a time when the United States Administration appears to have decided (see page 188) that the time has come for yet another spurt of technological innovation.

The second important lesson to be learned from the collapse of Rolls-Royce is that companies which operate in technically advanced fields should in future be more prudent. The contract to develop and manufacture the RB-211 for the Lockheed Company was, in retrospect, a disaster. When it was signed in 1968 nobody can have had reason confidently to calculate the cost of development and, by extension, the time likely to be taken for



development and the cost of the finished product. Arguing that if it somehow failed to win the Lockheed business, Rolls-Royce might have to abandon the manufacture of aircraft engines, the company set out to win the only customer in sight and, in the end, jubilantly signed a contract that was a simple financial trap. As things have turned out, it would have been far better if Rolls-Royce had said, in 1968, that the prospects for continuing business in aircraft engine manufacture were so bleak that it had better concentrate some of its technical resources on other kinds of products. What, after all, is the point of being the best manufacturer of steam railway locomotives when diesels are all the rage?

In the long post mortem on the Rolls-Royce bankruptcy, it has been fashionable to say that the company's technical management was too sure of itself and arrogant as well, although it is hard to see how these people could have behaved otherwise when they were locked into a contract which implied that failure would be avoided only by the most daring feats of technological brilliance. The more serious complaint is that nobody seems to have given sufficient thought to the long-term future of the company. Was it really sensible to plan for continued growth in a market in which the demand had levelled off? The most serious error at Rolls-Royce, which other companies in advanced technology should take to heart, is that it must frequently be necessary to redeploy skills from one field to another.

Catastrophe or Change?

PREDICTABLY (see *Nature*, 235, 63; 1972), anxiety about environmental catastrophe has spread to Britain, and it is hard not to remember Professor D. J. Bogue's description of the same phenomenon in the United States as the "nonsense explosion". Many readers of *Nature* appear to have been surprised that a journal which counts Sir Julian Huxley's grandfather as one of its sponsors should have taken such a fierce line on the warnings of environmental catastrophe now commonly to be heard. The truth is that public confusion which has been created in the past few years by warnings of catastrophe is a serious impediment to the rational conduct of society. A part of the difficulty is technical, for whether the prophets are complaining of the hazards of DDT, carbon dioxide in the environment, the threatened exhaustion of natural resources or the growth of population, a proper understanding of what happens and is likely to happen is fraught with uncertainty, complexity and error. Understandably, people at large are puzzled to know what weight to give to warnings of catastrophe around the corner and to assurances that the problems are not nearly as alarming as they are said to be. In the hope of contributing to public enlightenment, *Nature* will in the next few months publish a series of special articles written so as to put some of the environmental questions now widely talked of in what may be thought to be a better perspec-

tive. *Nature* will also organize a scientific conference with the Royal Institution on April 28 to provide a platform for moderate views and a discussion of them.

The question whether the years immediately ahead will bring catastrophe is, however, not so much technical as philosophical. The document published two weeks ago by *The Ecologist* says that "the principal defect of the industrial way of life . . . is that it is not sustainable. Its termination within the lifetime of somebody born today is inevitable—unless it continues to be sustained for a while longer by an entrenched minority at the cost of imposing great suffering on the rest of mankind". The calculations supposedly implicit in statements like this are that particular resources, petroleum for example, may be seriously depleted on time scales of the order of a century, or that, after a century of unrestricted growth, the population of the world may have grown to such a point that life is intolerable or even insupportable. As yardsticks which show what kinds of problems may in future be important, pieces of arithmetic like this are no doubt of some value. The error in supposing that they constitute a proof of imminent calamity is the assumption that administrative and social mechanisms which exist already or which are in the course of being developed will do nothing to fend them off, but this is to ignore the beneficent tendencies already apparent—the rapid decline of fertility in the past decade in South-East Asia and the Caribbean and the working of the classical economic laws of scarcity, originally described by the great Victorians, to strike a balance between exploitation and conservation and the way in which governments in North America and Western Europe have succeeded in improving the quality of urban air and water by laying out money on pollution control. In short, those who prophesy disaster a century or more from now and ask for apocalyptic remedies overlook the way in which important social changes have historically been effected by the accumulation of more modest humane innovations.

In the circumstances, it is not surprising that the remedies suggested for the avoidance of catastrophe are often unpleasantly unrealistic. *The Ecologist's* manifesto may be controversial because of its over-sharp definition of the supposed threat, but it shares with other declarations of this kind the advocacy of thoroughly pernicious changes in the structure of society. It is tempting to ask how many of those who gave their names to the document solemnly consider that industrialized societies such as Britain will be better off if they are organized in small communities in which social mobility is deliberately restricted and in which agriculture is central to everybody's life. Are these not potentially illiberal arrangements? Is there not a serious danger that to strive for them will weaken the will of civilized communities, developed and developing, to work towards humane goals—the removal of poverty and the liberty of the subject?

Strengthening the Guild

LORD JAMES's committee on teacher training, which has reported this week (see page 186), appears to have been as conservative as its critics expected and as predictable as the flow of inspired leaks to the newspapers in the past year has suggested. The essence of the committee's recommendations is that the British government should make the fullest use of the institutions of higher educa-

***Nature* and the Environment**

Nature and the Royal Institution will hold a scientific conference on environmental problems at the Royal Institution on the afternoon of Friday, April 28. Speakers and other details will be announced later.

tion and teacher training which exist at present, and to that extent the committee has fought shy of radical proposals. Its strongest set of recommendations is for the institutionalization of in-service training. In the past few years, local authorities and the Department of Education and Science have done a good deal to improve facilities for in-service training, mainly by the setting up of teachers' centres and by the provision of courses for those who want to go on them—a sub-population of the British teaching profession which tends to be over-representative of those who like attending courses and those who are already so skilled that they are less in need of in-service training than most others. Whether in practice the government will provide the resources, people as well as money, to allow for regular bouts of in-service training for all professional people is another matter.

In at least three respects, however, the James committee has fudged important issues. In the past few years, it has become apparent that the teacher training establishments, colleges of education as they are called, are often not educationally viable. The best among them have for several years been complaining of the difficulty of providing a broad and challenging curriculum for young men and women of 18 who think they might at some later stage become teachers but who cannot, in the nature of things, be sure. In circumstances like these, would it not be prudent to pay more serious attention than the James committee has done to the forging of such powerful links between the colleges of education and other establishments of higher education, polytechnics or universities, that students would be able to move freely from one institution to another and in such a way that it is no shame for a student to decide that he is not a teacher after all? The loose association of universities, polytechnics and colleges of education as members of the regional councils will not do.

The second defect of the report is its casual acceptance of the hypothesis that the supply of teachers for British schools is in principle unlimited. It is true, of course, that the remarkable expansion of British education in the years since 1945 has been predicated on the assumption that it is necessary merely to make teaching a more attractive profession to recruit the men and women needed to educate still larger numbers of children. Unhappily, however, the past few years have shown quite clearly that even if all teachers are, in terms approved of by the National Union of Teachers, equal, some are more equal than others. One unhappy consequence is the emergence of a more recognizable pecking order among schools, especially secondary schools, than is good for the future of the educational system and for the young people with whom it deals. In circumstances like these, is it wise to divorce the planning of facilities for teacher training from a consideration of how teaching should be carried out as completely as the James committee appears to have done? And is it not conceivable that Britain and many other countries similarly placed may be running into the kind of trouble which Mr Ivan Illyich has been describing in the context of developing societies? It is possible that with present techniques, countries such as Britain may find themselves unable to recruit the kinds of teachers on whom continued expansion of the educational system as it is at present must be based?

The third serious gap in the James committee's arguments is, in this sense, especially damaging. Over the years, the National Union of Teachers has been campaign-

ing for equality among teachers in all kinds of schools and for the recognition that a course of teacher training is a necessary qualification for the profession. Mr Edward Short, Secretary of State for Education and Science in the previous government, was the first to accept this argument, and the present government has, without saying as much, endorsed that decision. The result, of course, is that it is exceedingly difficult to exploit the contributions to British school education that might be made by men and women trained originally in quite different professions. Although the institutional framework which the James committee now puts forward will still allow people with first degrees in, say, physics to take up teaching as a career, the chances are smaller than in the past that people with advanced degrees in science and technology will find their way into the schools. Moreover, the recognition of teaching training as a necessary qualification for the schools will increase the difficulty of using part-timers from other professions, and the results are likely to be most damaging of all in those fields such as science and mathematics where the normal supply of teachers is inadequate.

100 Years Ago



WAITING FOR THE ECLIPSE

From *Nature*, 5, 266, February 1, 1872

OLD WORLD

TEACHERS

James on Training

AS widely expected, Lord James's committee on teacher education and training has put forward the suggestion that those who now attend colleges of education and education departments of polytechnics should take a preliminary two year course leading to a diploma in higher education (*Teacher Education and Training*, HMSO, 1972; £0.85). They would then start another two year course of an essentially vocational nature which would culminate in the award of the degree of BA (Education).

The basis of the committee's recommendations is that the education and training of all teachers should be regarded as a process of three stages—which the committee calls cycles. The first would be the personal higher education of the student, and the higher education diploma would be one of several awards, including university or CNAA degrees and some other specialist qualifications, that would be recognized as evidence of fitness to enter the second cycle—two years of professional preparation for a teaching career. The third cycle would involve refresher courses—at least twelve weeks in seven years—for teachers in mid-career.

The course followed during the first year of the second cycle would in many ways be similar to that now offered to graduates by university departments of education, comprising theoretical studies of education and practical teaching for a continuous period of at least four weeks. Half-way through the second cycle, successful students would be dubbed "licensed teachers" and would then take up their first salaried posts. The remainder of the second cycle would be the same as the existing probationary year during which the student teaches in a school. The James committee recommends that the probationary year should become an integral part of the training process and should involve the new teacher's attendance (for at least one day a week) at a centre where he would follow a course planned by his school and the centre. At the end of this time the licensed teacher would then become a "registered teacher" and be awarded a new professional degree, BA (Education).

In spite of the importance which the committee clearly attaches to the first two cycles of teacher training and education, it is the recommendations made in connexion with the third cycle—the in-service training of teachers—that pave the way for the remainder of the report. In-service training, says the committee, should be available to all schoolteachers and full-time staff in

colleges of further education to the extent of at least one school term in every seven years of service (reducing as soon as practicable to five years). Such training would not only serve to keep teachers abreast of new books, materials and equipment, but also of the results of educational research. The introduction of modern mathematics, and the development of science and French in primary schools, are also cited as situations demanding a coherent approach to the continuing training of teachers.

In order to service both third cycle training and the training of teachers when they are licensed teachers, the committee proposes the setting up of professional centres which would include the present colleges and departments of education and, possibly, some others based on existing teachers' centres. Every school and further education college would also appoint a professional tutor with responsibilities for the coordination of all second and third cycle training.

The committee recommends that the system should be administered by about fifteen Regional Councils for Colleges and Departments of Education, which would represent all educational interests including teachers themselves and local education authorities—within their regions. At a national level, there would be a National Council for Teacher Education and Training which would devise guidelines for the regional bodies, as well as watching over all professional teaching qualifications.

The report envisages a degree of MA (Education) for a few holders of BA (Education) degrees that would be obtained by studying for a further year at the end of the second cycle or later. It also advocates the increasing adoption of the BEd degree as an in-service qualification rather than one to be obtained at the outset of a teaching career.

ENVIRONMENT

A Watch on the World

THE establishment of a permanent global monitoring system and of a United Nations agency to coordinate monitoring and help to define international environmental policy are the chief recommendations in a report published last week by the Scientific Committee on Problems of the Environment (SCOPE), a committee of the International Council of Scientific Unions.

SCOPE's report, entitled *Global Environmental Monitoring*, is made at the request of the UN Conference on the Human Environment, due to meet in Stockholm in June this year provided the diplomatic squabbles which threaten the conference are cleared up.

SCOPE concludes that the basic en-

vironmental problems "result from adverse side-effects of advancing technologies and from the increasing rate of exploitation and unwise use of natural resources". While the committee feels that our present understanding of the large-scale processes in the biosphere is inadequate, it concludes that a "global environmental monitoring system is desirable, timely and feasible".

The report makes eighteen recommendations, the substance of which is that a global environmental monitoring system should be created by international cooperation based on national efforts. To ensure this, at least ten baseline stations should be established at a distance of 100 kilometres from the nearest large centre of population. A basic programme of research is outlined for these, to include assessments of atmospheric turbidity and carbon dioxide, studies of solar radiation and standard meteorological data, and assessments of the degree of pollution in all media by mercury, lead, cadmium, DDT and polychlorinated biphenyls.

A further 100 regional stations should be established. These should be fairly remote from large amounts of contamination, but will give a guide to environmental quality in settled regions of the world. SCOPE hopes that every country will be invited to provide these centres, the larger countries providing up to ten such stations. Their basic monitoring programmes should cover the same field as the baseline stations. Finally, SCOPE recommends the establishment of about thirty stations in areas of high contamination to investigate the link between high levels of contamination and their effect on human health and biological systems.

The monitoring programmes for the stations should be flexible, so that other potentially harmful substances and phenomena can be studied.

Astronomy

THE Royal Astronomical Society's Gold Medals have been awarded to Professor Fritz Zwicky and Dr H. I. S. Thirlaway. Professor Zwicky's award is for "his many distinguished contributions to an understanding of the constituents of the Galaxy and the universe". Dr Thirlaway's award is for "his distinguished work in geophysics and for advancing seismological knowledge relating to earthquakes and explosions". Professor Paul Leddox is awarded the Eddington Medal of the society for his "theoretical studies of stellar stability and the properties of variable stars".

SCOPE also wants to see at least two International Research Reference Stations established, one at least in a tropical area. The purpose of these should be partly to monitor (as with the other stations), but also to determine other substances for measurement and to develop standard methods for the measurement.

These stations are all land based. SCOPE recommends that pilot studies be undertaken before a full programme gets under way in marine environments. It recommends the North Sea, Baltic Sea, Mediterranean and Puget Sound as the first areas for study. From these beginnings, and other national programmes, a world monitoring programme can be built up.

To ensure unity of approach, SCOPE recommends that an operations manual should be prepared and a Central Monitoring Coordinating Unit established. This would plan and run the monitoring programmes, collate the results, standardize observations and report to the United Nations. The actual data can be stored in a number of centres, some based on ones already in existence, with a strong effort made between them for cooperation.

The report has nothing to say on how the information the monitoring system will obtain should be applied to prevent damage to the environment. It does, however, acknowledge that monitoring is only part of the environmental problem and it does urge the United Nations to consider establishing an international unit to coordinate monitoring, research and policies.

Although the problem is global, SCOPE sees individual nations being responsible for various parts of the monitoring programme and it recommends that the United Nations and its agencies, other relevant organizations and the Central Monitoring Coordinating Unit should meet to "formulate, define and assign responsibility for individual contributions to a practicable and unitary monitoring programme".

SCIENCE POLICY

Another Assault

LORD ROTHSCHILD'S proposals on the future organization of the British Government's research and development activities came in for more heavy criticism at a meeting of the Science Policy Foundation last week.

His report, published last November in a green paper together with the Council for Scientific Policy's views on the research council system, was criticized for vagueness, for not properly considering the function of the research councils, for being too limited in its scope, for being better on paper than it was likely to prove in practice, and for putting control of science too closely into the hands of government—against

the recommendations of the Trend committee eight years ago. At the same time, the government was criticized for accepting the customer-contractor principle without discussion and for allowing too short a time for discussion of the reports.

But while there was much voluble criticism, the attitude of the conference was not all negative. Many participants clearly agreed with Lord Shackleton who said that Lord Rothschild had stated a basic truth in his customer-contractor principle, but he doubted if government departments have the capability to become as efficient and well informed a set of customers as Lord Rothschild envisages. Fears were expressed that the government would accept the Rothschild report without any trial period to see if his recommendations really could be put into practice, and it was felt that there is a real danger that science will be left trying to operate a customer-contractor principle with unintelligent customers. It was also suggested that the fears caused by the imprecision of the report, if repeated often enough, might become facts.

To some, however, Rothschild's proposals are not entirely welcome but do open up some exciting possibilities. The interchange between government, industry and universities would be improved and the seconding of scientists to work with Rothschild's proposed Chief Scientist would not only provide the departments with scientific foresight but would also give scientists experience of the real world of hard decision taking.

Dr Walter Marshall, director of the Atomic Energy Research Establishment at Harwell, described his establishment as a "multi-functional" laboratory, and produced a breakdown of its expenditure to show that much of Harwell's

work already fits Lord Rothschild's customer-contractor principle. By 1975-67, he thought that 45 per cent of his laboratory's income would come from contracts. He warned, however, that almost one-fifth of the laboratory's work is long-term industrial research, for which there is no immediate customer, but for which customers can be found once industry has become accustomed to the ideas being offered it. This work, said Dr Marshall, can be justified over a period of years, but no researcher could be held accountable for it on a month by month or annual basis. And it is precisely this work which might suffer if the customer-contractor principle is too firmly enforced.

Overall, in spite of the battering to which the report was subjected, it was felt within the meeting that some of Lord Rothschild's recommendations for accountability and for a scientifically aware civil service were all to the good, providing that the changes were introduced slowly, preferably with an experimental period.

But Lord Rothschild's suggestion for hiving off money from the research councils and placing it in the hands of the departments was heavily criticized. It was clearly felt that under this arrangement the days of the research councils would be numbered as they would lack sufficient size to operate effectively. The fears were greatest for the future of the Natural Environment Research Council.

As a framework for stimulating discussion and self-examination, the report was clearly felt to be valuable, but as a framework for action it was felt to be too ill-defined. Its underlying principle that researchers should be accountable was approved, but the details of Lord Rothschild's attempts to enforce that principle were not.

R and D and the Select Committee

THE Select Committee on Science and Technology is to hold a series of public meetings as part of its investigation into the government's policy on research and development. One of the foundation stones of their investigation is the green paper that contains the reports of the Council for Scientific Policy on the future of the research council system and Lord Rothschild's report on the organization and management of government research and development. The following people will give evidence to the select committee in committee room 15 of the House of Commons on the dates shown.

January 26	Lord Rothschild.
February 2	Sir Frederick Dainton.
February 9	Sir Alan Hodgkin.
February 16	The Duke of Northumberland and members of the MRC.
February 23	The Hon. J. J. Astor and members of the ARC.
March 1	Professor F. H. Stewart and members of the NERC.
March 8	Professor Sir Brian Flowers and members of the SRC.
March 15	Professor R. C. O. Matthews and members of the SSRC.

Mrs Margaret Thatcher and Lord Jellicoe will also give evidence to the select committee on dates to be arranged.

NEW WORLD

Domestic Problems Shape Science Budget

by our Washington Correspondent

FOR the second year in succession, President Nixon has sent to Congress a budget calling for substantial increases in spending on science and technology. Put in their best light, the sums of money being requested for research and development for the 1973 fiscal year (which runs from July 1, 1972) add up to \$17,819 million—an increase of about 8.4 per cent compared with corresponding figures for 1972. But not all the money being requested for 1973 will be spent in that year, and the actual sum available for science and technology will be barely sufficient to keep pace with inflation.

Clearly stamped on the new budget is the Administration's desire to channel science and technology to help solve pressing national problems—for large domestic projects, such as the development of sources of clean energy and better transportation, carry off the bulk of the \$700 million increase earmarked for civilian research and development. The policy for science and technology which emerged in the 1972 budget, and which has been underlined in the new budget, is to allow modest increases in selected areas of basic research but to hold down overall expansion as far as possible. The areas of the scientific enterprise that benefit from this policy are chiefly those that hold promise of social or economic return.

The 1973 budget does, nevertheless, carry through the upswing in federal science funding begun last year, and overall increases in obligations for science and technology are again almost reminiscent of the golden days of the early 1960s. Proposed obligations for research and development in the universities are up by 12 per cent, to \$2,257 million. Defence research and development has again picked up a massive \$800 million increase, to \$9,400 million—again more than half the total proposed for science and technology—while civilian projects, exclusive of defence and space, are set to increase by \$700 million, or 15 per cent. The only activity to show a decline is space research and development, but even that is being kept approximately constant, thereby confounding the worst fears voiced in recent weeks.

As for individual agencies, the National Science Foundation is again set for a substantial increase. Its proposed budget climbs to \$674.7 million, \$21.7 million of which is composed of funds carried over from previous years,

while \$653 million is new money. The science, although its total education budget is increased, and although high energy physics has been given its first budget increase since the mid-1960s, nearly all the extra money is earmarked for the National Accelerator Laboratory, while other installations again have to be content with about the same helping as they received in 1972. But on the plus side, the green light has at last been given for construction of the Very Large Array, on which the radio astronomy community has set its sights for the past decade, and last year's frenzied political activity surrounding cancer research has been translated into an extra \$93 million in the budget of the National Cancer Institute.

Although the science budget is less rosy than it appears at first sight, what increases there are can be laid chiefly at the door of the Administration's recent efforts to uncover social projects ripe for study by the scientific community. According to Dr Edward E. David Jr, the President's Science Adviser, the 1973 science budget represents a strategic plan designed to give greater coherence to federal research and development efforts, and it draws heavily on the efforts by William M. Magruder and the domestic council to seek out so-called technological initiatives (see *Nature*, 234, 179; 1971). This means in effect that of the extra \$700 million devoted to civilian research, some \$450 million is earmarked for projects aimed at developing fast, pollution-free transportation, sources of clean energy, reducing loss of life from natural disasters, studying the health effects of pollutants, solving urban social problems and eliciting

These sums are, however, far from being guaranteed. For one thing, the Administration's budget must now be chewed over by a Congress whose legislative timetable and actions will be shaped by the elections, but more importantly, the sums of money represent obligations and not actual expenditures. There is often a lag of two or three years between the time when money is allocated and when it is actually spent. Thus, although total obligations for research and development are expected to rise by some 8.4 per cent, expenditure in 1973 is set to increase by only about 4.5 per cent, which is insufficient to keep pace with inflation (see table 1). By the same token, research in colleges and universities will increase by 9.7 per cent, while obligations are expected to rise by 12 per cent.

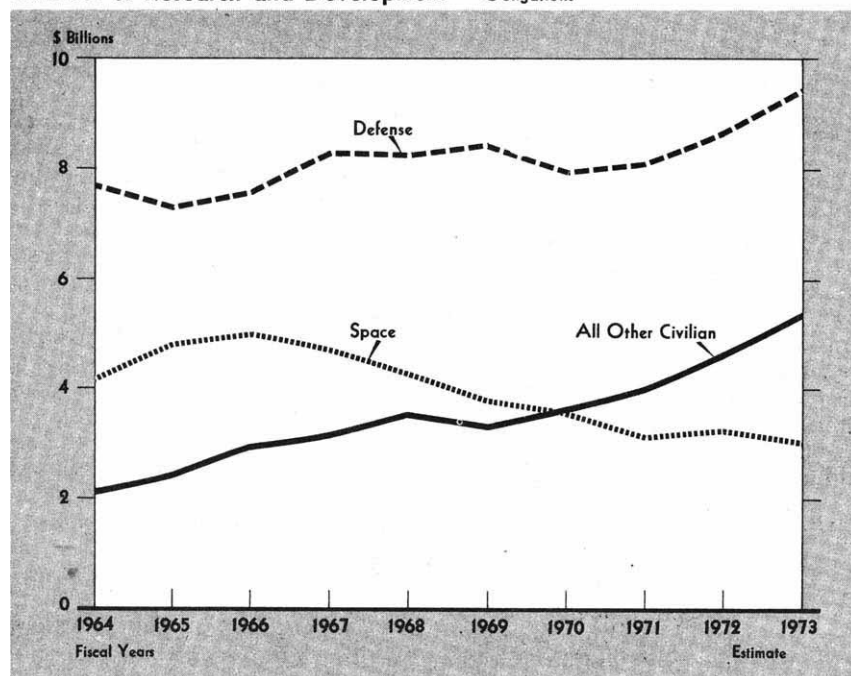
Budgetary restrictions have also forced the termination of some scientific projects. The Grand Tour of the outer planets, originally scheduled to be launched in the late 1970s, has been scrapped, and development of the NERVA nuclear powered rocket has finally been aborted. The National Science Foundation is again cutting back on its graduate traineeships in

the science, although its total education budget is increased, and although high energy physics has been given its first budget increase since the mid-1960s, nearly all the extra money is earmarked for the National Accelerator Laboratory, while other installations again have to be content with about the same helping as they received in 1972. But on the plus side, the green light has at last been given for construction of the Very Large Array, on which the radio astronomy community has set its sights for the past decade, and last year's frenzied political activity surrounding cancer research has been translated into an extra \$93 million in the budget of the National Cancer Institute.

Table 1 Conduct of Research and Development (in millions of Dollars)

Department or agency	Obligations			Expenditures		
	1971 actual	1972 estimate	1973 estimate	1971 actual	1972 estimate	1973 estimate
Defence—Military functions	7,423	8,013	8,756	7,541	8,031	8,177
National Aeronautics and Space Administration	3,284	3,327	3,302	3,337	3,137	3,131
Health, Education, and Welfare	1,466	1,769	2,012	1,288	1,450	1,708
Atomic Energy Commission	1,303	1,308	1,375	1,303	1,308	1,375
National Science Foundation	337	453	525	335	409	455
Transportation	220	296	380	198	233	282
Agriculture	318	356	370	315	349	359
Interior	185	216	250	175	212	238
Commerce	143	169	229	114	146	192
Environmental Protection Agency	137	176	168	101	157	174
Veterans Administration	64	70	78	61	66	73
Office of Economic Opportunity	84	50	78	75	70	65
Postal Service	40	68	74	34	39	64
Housing and Urban Development	48	53	63	40	56	54
Justice	10	27	30	9	20	26
Labour	23	27	31	22	26	30
Smithsonian Institution	17	23	29	17	22	28
All other	42	48	52	40	48	49
Total	15,143	16,447	17,819	15,005	15,779	16,480

Conduct of Research and Development — Obligations



ing information about how industrial research can best be stimulated. Add to this figure the \$93 million increase for cancer research, and there is not much change from the \$700 million gleefully being held up by the Administration as proof of its commitment to research and development.

But there may be even more money on the way for similar technological projects aimed at improving the quality of life, reducing unemployment or stimulating the economy, for President Nixon disclosed in his State of the Union Message (the statement outlining the Administration's legislative proposals for the coming year which was delivered to Congress last week) that a special Presidential message on technology will soon be presented to Congress. Although Dr David said last week that no decision has yet been made on whether more money will be asked for the technological initiatives project hammered out between his Office of Science and Technology and Magruder's office, it seems clear that technological initiatives will form a large part of the promised Presidential message.

As for basic research, Dr David said last week that "even as increasing attention is paid to problem-oriented efforts, funding for high energy physics will go up by \$10 million in fiscal year 1973, and R&D in the Universities will, in the overall, go up 12 per cent or \$237 million to \$2,257 million." Fundamental research supported by the National Science Foundation is also set to increase by 10 per cent, and spending on biomedical research is given a 12 per cent increase.

But even these proposed increases are not as generous as they seem at first

sight. Of the \$10 million increase in the high energy physics budget, for example, the 200 BeV accelerator takes \$6.5 million, and several other installations are either being held constant or may even have their budgets cut by a few thousand dollars. And as for the \$140 million increase in the budgets of the institutes and divisions of the National Institutes of Health, \$93 million goes to cancer research and \$22 million goes to the National Heart and Lung Institute for programmes aimed at cardiovascular, sickle cell and lung disease.

Research on cardiovascular diseases threatens to be the chief health research crusade of this year, just as cancer research was the political crusade last year. In his State of the Union message, for example, President Nixon announced that he would soon "assign a panel of experts to help us determine why heart disease is so prevalent and what we can do about it", notwithstanding the fact that a major report on just that subject was recently published by the National Heart and Lung Institute. But Senator Walter Mondale has already got off the mark with a bill calling for \$2,500 million to be spent over the next five years on research into cardiovascular, blood and lung disease, and for the development of bioengineering related to such diseases. The \$22 million being asked for the National Heart and Lung Institute may thus prove insufficient to buy off the crusaders.

This year, budgetary increases for science form part of an expansionist budget designed to curb unemployment. If Mr Nixon's economic strategies do not have the desired effect, and if the

deficit reaches a politically unacceptable amount, a return to the era of balanced budgets may severely squeeze the scientific effort. What Congress will do to the budget during the annual appropriations ritual is also a moot point, but it is clear that if funding for basic science, as opposed to civilian technological projects, is cut back even slightly, funding increases could easily be swallowed up by inflation.

Hard Times for Space

from our Washington Correspondent

THE extent to which the National Aeronautics and Space Administration has staked its future on the space shuttle is evident from its budget requests for the 1973 financial year. Although the request for funding for the shuttle amounts to only \$200 million for 1973, the modified version of the project, which was recently given President Nixon's personal support (see *Nature*, 235, 68; 1972), is expected to become the agency's most important programme when the two remaining Apollo projects are completed this year. Other projects, notably the proposed Grand Tour of the outer planets and the development of the NERVA nuclear powered space vehicle, both of which are to be scrapped, are less fortunate.

NASA's budget request for 1973 involves total obligations of \$3,200 million—essentially the same level as the requests for 1972. But inside the global budget there has been considerable changes in budgetary levels for individual projects, and once again, there is considerable emphasis on projects likely to benefit mankind. As far as manned space flight is concerned, funding for the Apollo programme (which will be completed later this year with Apollo 17, for which funds have been provided) will begin to dry up while funds for Skylab increase. Later, as development costs on Skylab begin to tail off, funding for the shuttle will begin to grow, but according to Dr George Low, Deputy Administrator of NASA, peak funding for manned space flight will not grow much above present levels.

As for space science, considerable funding increases are proposed for 1973; the total budget request is \$669.4 million, compared with \$552.9 million for 1972. The chief changes are that the Grand Tour has been scrapped in favour of more intensive study of Jupiter and possibly Saturn, but details of the programme will be worked out soon in time to influence funding for the 1974 budget. Such missions will, however, almost certainly depend on Pioneer or Mariner spacecraft. Another casualty is the Orbiting

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION
Research and Development Programmes—Budget Plan

(Thousands of dollars)

	FY 1971	FY 1972	FY 1973
Manned Space Flight	1,422,469	1,285,475	1,224,400
Apollo	913,669	601,200	128,700
Space flight operations	507,300	682,775	1,094,200
Advanced missions	1,500	1,500	1,500
Space Science	398,654	552,900	669,400
Physics and astronomy	115,956	110,100	156,600
Lunar and planetary exploration	144,900	291,500	321,200
Bioscience	12,898	—	—
Launch vehicle procurement	124,900	151,300	191,600
Applications	166,960	187,500	194,700
Space applications	166,960	187,500	194,700
Aeronautics and Space Technology	260,336	212,825	249,340
Aeronautical research and technology	100,132	110,000	163,440
Space research and technology	105,004	75,105	64,760
Nuclear power and propulsion	55,200	27,720	21,100
Tracking and Data Acquisition	289,943	264,000	259,100
Technology Utilization	4,000	5,000	4,000
Total	2,542,362	2,507,700	2,600,900

Solar Observatory Programme—OSOs J and K have been scrapped for budgetary reasons. On the other hand, however, a substantial increase is being proposed for the high energy astronomy observatories, which are down for \$59.6 million in 1973, and the Viking programme which is scheduled to get \$229.5 million.

The NERVA programme has again been subjected to the budgetary axe, but this year instead of merely cutting the programme, the Administration is asking for its total extinction. So far, NASA and the Atomic Energy Commission between them have pumped \$1,400 million into the project, but it has now been decided that the research should give way to research on a smaller nuclear electric system which would provide the capability of reaching the outermost planets in the 1980s. The NERVA programme is, however, a perennial favourite of Congressional supporters of space research, and it is very likely that the authorizations committees will again try to keep the project going. Last year, when the Administration only provided just enough funds to keep NERVA going, Congress increased the appropriations, only to have the Office of Management and Budget withhold the increase.

NATIONAL SCIENCE FOUNDATION

New Directions

By our Washington Correspondent

In tune with the policy of funding scientific activities that are likely to be socially useful, the budget of the National Science Foundation shows significant increases in the amount of money requested for the support of applied research. Also included in the budget are funds for eliciting information on the process by which basic research is ultimately transformed into

marketable products or into growth in GNP, and another large new project will be concerned with finding methods for stimulating non-governmental research and development. But in spite of these new directions, the largest single programme increase for the NSF is for support of basic research.

Overall, the foundation's budget request amounts to \$674.7 million, which includes \$21.7 million carried over from 1972 in unallocated funds. New appropriations amount to \$653 million, compared with the total of \$622 million appropriated for 1972. Of these funds, scientific project support is set to take \$275.3 million, and some 7,400 faculty scientists and 7,000 graduate students are expected to benefit from the 6,200 grants that the foundation hopes to distribute. This project support request represents an increase of some \$28.7 million compared with the foundation's budget for 1972. But even in this category, the foundation emphasizes, in a statement explaining its 1973 budget request, that attention will be given "to those areas where new knowledge and understanding can lead to opportunities for solution of social, environmental and engineering problems".

Perhaps the most significant item in the NSF's requests for support of basic research is the \$3 million earmarked for a start to be made on the Very Large Array antenna system. Radio astronomers have lobbied for the telescope array for the best part of a decade without success and, although no decision has yet been taken about where the VLA will be situated, Arizona seems to be the favourite among some astronomers. The radio telescope at Arecibo is scheduled to receive \$3.3 million, slightly less than last year when the budget request included funds for resurfacing the dish, the Kitt Peak National Observatory is down for \$8.2 million, the National Radio Astronomy

Observatory is to receive \$7,200 in addition to the \$3 million set aside for the VLA and the National Center for Atmospheric Research is set to receive \$17.9 million.

The programme of Research Applied to National Needs, a set of projects which have the potential for increasing economic productivity or which have potential social applications, is down to receive \$80 million. This request is about the same as the foundation asked for last year, but Congress took a dislike to the programme, chopped some \$26 million from the request and put the money into the foundation's education support programmes. This year, the RANN programme has been expanded to take in research on solar energy, earthquake research and tunnelling technology—projects which may win more favour with Congress than the RANN programme has earned in the past.

What annoyed Congress last year was that the NSF had cut its budgets for student and institutional support, while at the same time increasing its requests for the RANN programme, a situation which drew from the House Appropriations committee the tart remark: "The committee will expect the foundation to utilize the funds included for science education support and for institutional support for science as recommended, instead of the diversion of additional funds to basic or applied research". The foundation had little chance to divert funds from education, because the Office of Management and Budget withheld much of them, and the NSF is again asking for reductions in its institutional and graduate support funds. Funds for science education improvement are, however, increased by \$3.9 million.

Another significant new programme to be conducted jointly by the National Science Foundation and the National Bureau of Standards is aimed at finding out how non-federal investment in research and development can be stimulated. The foundation is requesting \$22 million for this purpose, which will be spent on trial projects to explore such devices as cooperative undertakings between industry and universities, new institutional arrangements and other mechanisms. The NSF's stake in the enterprise will be confined chiefly to long-term research projects, while the National Bureau of Standards is asking for \$18 million to stimulate the marketing end of the innovation spectrum.

As Dr William D. McElroy, who leaves the directorship of the NSF on February 1, remarked last week, the foundation has changed markedly from three years ago, when it was concerned almost exclusively with basic research and education.

Health and the Medical Research Council

Dr M. F. Perutz, chairman of the governing board of the MRC Molecular Biology Laboratory, Cambridge, offers his views on the Rothschild report.

THE Rothschild report carries the implication that the Medical Research Council lives in an ivory tower, that it fails to coordinate its work with that of government departments and does not give the country value for money in terms of human health. It has also been said that the MRC has done well in supporting molecular biology but has achieved little else of significance. I wish to show that the research supported by the MRC has brought medical and economic benefits large in proportion to its cost and that its high productivity and cost-effectiveness have been the result of a scientific policy which implementation of Lord Rothschild's principal proposal may jeopardize.

I wish first to comment on the alleged lack of coordination with the Departments of Health. In matters relating to clinical medicine, the council is advised by a Clinical Research Board five of whose twelve members are nominated by the health departments and on which also sit health department assessors. Of the forty-three committees advising the council on specialized aspects of medicine, three are joint with the Department of Health and Social Security (DHSS) and on nearly two-thirds of them the health departments are represented by members or observers. There is daily contact and collaboration between the MRC and the DHSS at many levels. Important practical studies have been done by the MRC together with the DHSS, including the trials of poliomyelitis, measles and BCG antituberculosis vaccines. The MRC and DHSS also run a joint research unit for Epidemiology and Medical Care.

The complaint of non-cooperation in the field of epidemiology and prophylactic medicine is particularly surprising. In fact, it is in epidemiology that governments have failed for many years to put one of the MRC's most far-reaching discoveries into effect. In 1950 A. Bradford Hill and R. Doll presented the first evidence of the connexion between smoking and lung cancer. By 1957 the MRC reached the conclusion that smoking, and particularly cigarette smoking, was the principal cause of the disease, but this was widely disparaged and evaded because the evidence was "only" statistical. Since then, even the tobacco industry has had to accept it, and

300,000 people in Britain have died from lung cancer, more than all the British soldiers killed in the Second World War. If a prompt campaign against smoking had been able to save only a fraction of these victims, it would have been enormously worth while.

One of the most original contributions to epidemiology was made by J. N. Morris of the Social Medicine Research Unit. He showed in 1951 that the mortality from a first episode of coronary disease in London bus drivers was twice that in conductors, and in Post Office clerks twice that in postmen. His was the first definitive evidence for the now well-established connexion between coronary mortality and lack of physical exercise, but again nothing was done to publicize it widely.

M. M. Swann complained that the MRC spends too little on dental research, but in fact its Dental Research Unit has pinpointed the main cause of caries. In five-year-old children of the general population, the incidence of caries is five times greater than in dentists' children, who restrict their sugar intake between meals and clean their teeth after their last food at night. Swedish workers had shown that the number of new cavities per year is related to the amount of sugar consumed and to the frequency of its consumption. The unit confirmed this finding directly by applying sugar, or the acids derived from its bacterial decomposition, to teeth in the test-tube and showed that caries results. Fructose, the sugar of fruit, does not have this effect. It seems that great savings in the dental health service could be effected by propaganda to overcome the social prejudices against fluoridation of water supplies and depriving children of sweets.

The MRC's contributions to clinical medicine are outstanding. Until 1951 there was no treatment for high blood pressure. Then W. D. M. Paton and E. J. Zaimis of the National Institute for Medical Research produced an analogue of the alkaloid curarin which had the quite unexpected property of producing a fall in blood pressure. From this drug, the present substantial control of high blood pressure has developed.

Anxiety over radiation fallout after

the Second World War led to the setting up of a programme of research in radiobiology. Results obtained by W. M. Court-Brown and R. Doll proved that the risk of inducing leukaemia rose linearly with exposure to ionizing radiations and that there is no evidence for a safe threshold of radiation damage. This helped to persuade the Great Powers to conclude the Atmospheric Test Ban Treaty. One of that programme's unplanned achievements was C. E. Ford's ingenious and simple method of making mammalian chromosomes clearly visible for the first time. This became the springboard for tremendous advances in human cell genetics, including the discovery of an extra chromosome in mongols (made independently by a group in Paris and an MRC Unit in Edinburgh) and the present method of detecting mongolism and other abnormalities in the womb.

Nobel Prizes, people now say, are a socially irrelevant luxury, but a closer look suggests that some of the MRC prize-winners' work has not been entirely useless. Transplantation of organs, for example, has become successful only through the development of methods for maximizing tissue compatibility and inhibiting graft rejection. The theoretical basis for the clinical procedures now used was largely laid by Sir Peter Medawar, who received the prize together with Sir MacFarlane Burnet, and by N. A. Mitchison, R. E. Billingham, N. F. A. Woodruff and others supported by the MRC.

In 1942 A. J. P. Martin and R. L. M. Synge, then at the Wool Research Station, invented liquid partition chromatography for which they received the Nobel Prize. Later, Martin, with A. T. James, while at the National Institute for Medical Research, invented gas chromatography. The two analytical methods have been of enormous medical and industrial value (especially to the oil industry). By increasing productivity and quality of known chemicals and facilitating the development of new ones they may have brought more income to this country than all the money ever spent on the MRC.

The same may be said of A. S. Parkes, E. J. C. Polge and Audrey Smith's discovery, also made at the National Institute, that sperm can be stored for long periods by freezing it in a diluting fluid containing glycerine. This opened the way to artificial insemination which has brought incalculable benefits to the breeding of livestock.

In 1953 E. P. Abraham and others at Oxford, together with members of

the MRC Antibiotics Research Station, isolated cephalosporin, an antibiotic with a wide spectrum of activity, including organisms resistant to penicillin. The lives saved by this drug cannot be counted, but the pounds earned can. So far the National Research Development Corporation has received nearly £9 million in royalties for its sale. Assuming a royalty of 15 per cent, the sales value covers the total cost of the MRC for the succeeding 12 years.

In spite of vaccination, tuberculosis remains a major health problem at home and a much greater one in the less developed countries where neither expensive drugs nor prolonged sanatorium treatment can be afforded. In 1956 the World Health Organization, the government of India and the MRC set up a tuberculosis chemotherapy centre in Madras, and entrusted its scientific direction to the MRC. The centre conducted carefully controlled trials of the relative efficacy of various drugs, and of the risks of spreading the infection, when patients were treated either in a sanatorium or while living at home. In the course of these trials the centre proved that treatment in a sanatorium offered no advantages over outpatient treatment. This project and others supported by the MRC also led to the development of the so-called "100 per cent effective drug regimens" which have now been internationally adopted. At current prices, the direct annual savings of these discoveries to the DHSS for the year 1968 compared with 1954 have been estimated as £50 million, quite apart from the benefits of increased production by the more rapidly cured patients.

The fight against leprosy has been extremely difficult, largely because the infection could not be reproduced experimentally in animals. After a decade of work R. J. W. Rees and others at the National Institute have now succeeded in reproducing all the features of the human disease in mice made immunologically incompetent. This is a tremendous breakthrough because for the first time drugs can be screened rapidly and possible methods of immunization tested.

The discoveries of practical value I have recounted are merely the tip of the iceberg, and they have been achieved by the MRC at a total budget of £150 million over the past 20 years. Regarded as a whole, the MRC's advances are comparable both in quality and quantity with those achieved at much greater cost by its American counterpart, the National Institutes of Health. How did the MRC manage to achieve so much on its small budget?

The council's policy is to support research in universities, hospitals and in its own laboratories; to seek out talented people and to give them scien-

tific freedom, but to subject the scale or continuation of support to periodic review (usually every three years) in the light of progress achieved; to initiate and give priority to research on socially urgent problems such as, currently, the causes and treatment of drug addiction, or reproductive physiology in relation to population growth; to regard basic and applied research as inseparable, because in medicine few applied problems can be solved without going back to fundamentals and basic research finds unexpected clinical applications; to take a long view of medicine, supporting not only research that is directly related to human disease, but biological and chemical work which is likely to lead to a deeper understanding of the human body and to form the scientific basis for future advances in diagnosis and therapy; and finally to be patient, because the benefits of medical research are often reaped only in the fullness of time.

In view of the MRC's great achievements, the government should avoid action that would impair the quality of work and the high morale of the staff. The Rothschild report contains several valuable suggestions for further strengthening the collaboration between the MRC and the Health Departments, but the principal proposal, which is to turn a large fraction of the MRC's budget over to project-oriented research done on a customer-contractor basis for the health departments, has aroused widespread anxiety and criticism. I share these misgivings because in medical research most of the fruitful ideas come from below, from individual scientists and doctors, rather than the ministry or the council. By forcing the council to direct a major effort to projects imposed from above, originality will be at a disadvantage and much money may be wasted on fruitless work of mediocre quality.

In conclusion I will cite three examples of research in progress. Sir Keith Joseph, Secretary of State at the DHSS, has recently announced that patients are to be transferred from large mental hospitals to psychiatric units in district general hospitals. How will this affect the patients? Workers at the MRC Social Psychiatry Unit are trying to discover how patients with chronic mental disorders react to environments such as hospital, hostel, day unit, workshop or home. Do some aspects of these environments prevent and others provoke schizophrenic symptoms? How do social interactions affect schizophrenics with disorder of thought and what effects do they have on the people around them? Of what value is preventive medication in these various situations? Many of these studies are being done on patients in the local London area, and their results can be used

directly for planning the psychiatric services there.

Young drivers have more accidents than adults and boys have twice as many as girls. The MRC Applied Psychology Unit has set out to study the contributions of attitudes and skills to the high accident rates of young drivers. This will be difficult to discover because in all normal tests of skill performance declines with age. How can one trace and quantify the speedbound boy's reckless impulse? And how can its ruinous effect be prevented?

In 1923, surgeons discovered that stimulation of the visual cortex through electrodes placed on it causes people to see spots of light. This suggested to G. S. Brindley, the director of the MRC Neurological Prostheses Unit, that it might be possible to implant an array of electrodes on a blind person's cortex linked to a receiver implanted in the head just under the scalp. Stimulation of a selected set of electrodes by a television camera and transmitter carried by the patient might then allow him to see patterns of light such as letters. This might be developed sufficiently to allow totally blind people to read and get about. After tests on baboons to check the harmlessness of the proposed implant, an array of 80 electrodes was implanted into a totally blind woman volunteer patient in July 1967. Stimulation through single electrodes produced sensations of spots of light in a specific position of the visual field, and stimulation of several electrodes made several spots appear simultaneously, so that patterns could be built up predictably.

A new and much improved device is now waiting to be implanted. Even if no more than 70 of its electrodes are capable of producing sensations of distinct spots, it should be possible to cause the patient to see single letters of the alphabet. In that case an attempt will be made to link this to a modified television camera so as to make it possible to read ordinary print. Motorcycle and car accidents often produce damage to the spinal cord which results in permanent paralysis of the limbs. Brindley plans to pick up signals in the motor cortex of the brain, amplify and recode them, and conduct them to spinal roots that innervate the paralysed muscles.

Critics attribute the passionate loyalty to the MRC which has been expressed by many scientists to their never having had it so good, but I believe that this loyalty springs chiefly from common pride in the MRC's achievements and appreciation of its imaginative policies. Given freedom of action and public support, the MRC may achieve many more great advances, such as healing the leper and making the blind man see and the lame one walk.

NEWS AND VIEWS

A Record Cosmic Ray Primary?

AN extremely large extensive air shower (EAS), caused by a cosmic ray particle incident on the atmosphere, has been observed by the air shower array of the Institute for Nuclear Study, University of Tokyo, and recently reported by K. Suga and colleagues (*Phys. Rev. Lett.*, **27**, 1604; 1971). Their analysis indicates that the total number of particles in the shower at sea level was $\sim 2 \times 10^{12}$. This suggests that the energy of the primary particle that produced the EAS was $\sim 4 \times 10^{21}$ eV.

The highest primary energies reported from other large EAS arrays have been $\sim 10^{20}$ eV at Volcano Ranch in the United States (J. Linsley, *Phys. Rev. Lett.*, **10**, 146; 1963), $\sim 10^{20}$ eV at Haverah Park, England (D. Andrews *et al.*, *Acta Phys.*, **29**, Suppl. 3, 343; 1970), and $\sim 2 \times 10^{20}$ eV at Narrabri, Australia (R. G. Brownlee *et al.*, *Acta Phys.*, **29**, Suppl. 3, 377; 1970). The Japanese thus claim that their event has at least ten times more energy than any cosmic ray primary observed previously. The presence of such particles in the universe, even with an extremely low flux, is of considerable astrophysical and cosmological importance. But the processes by which particles can be accelerated to these enormous energies are unknown. Suga and colleagues point out that the directions of a pulsar, AP 2015+28, and a radio source, 3C409, are inside the uncertainty of the arrival direction of their event ($\pm 4^\circ$). The direction of a cosmic ray proton of energy 4×10^{21} eV reaching the Earth from either of these sources would not be seriously affected by the intervening magnetic field.

Two chief problems arise in reaching an accurate value for the energy of the primary particle initiating an EAS. The central core of the EAS must be well located to enable the observed samples of particle density to be used to calculate accurately the total size of the shower. Certain assumptions must then be made about the nuclear processes in the atmosphere in order to obtain the relationship between shower size and primary energy.

The problem of the location of the core turns out to be the chief source of possible error. The density of particles falls off rapidly with distance R from the central core of the shower, roughly as $R^{-3.5}$. Thus an error in the location of the core can cause the size of the shower to be in error by a considerable amount. It has been pointed out that it is possible for large errors in the core location to occur if the core of the shower happens to land outside the perimeter of the detector array, such as is the case with the large event observed by the array at the Tokyo Institute for Nuclear Study.

At the time of the event three detector stations, each with a pair of 2-m² scintillators separated by 50 m, were being operated. The three stations made up a triangle with sides 1,890 m, 1,350 m and 850 m. A small but complex array of detectors, situated just inside one side of the triangle, 300 m from one of the stations, was also operating. This detector complex consisted of twenty-two unshielded scintillation detectors of 1 m² distributed over a circle of diameter 100 m, a 20-m² spark chamber

and two 8-m² scintillation detectors underground at a depth of 5 m and 15 m to observe muons with energies above 1.5 GeV and 5 GeV. This particular EAS gave particle densities of 36 ± 9 m⁻², 80 ± 6 m⁻² and greater than 281 m⁻² at the three outer detector stations and a density of $2,050 \pm 110$ m⁻² averaged across the 100 m of the small array of detectors.

The direction of arrival of the shower with respect to the Earth's surface could be classified as near vertical (zenith angle $\theta = 20 \pm 4^\circ$). The right ascension and declination of the arrival direction were $\alpha = 20$ h 14.5 min and $\delta = 24^\circ$.

The location of the centre of the shower on the ground was estimated by assuming a form for the lateral density distribution of charged particles away from the core and took into consideration that the range of observed densities across the small 100-m array was comparatively flat. Their analysis places the core some 690 m from the centre of the small EAS array and about the same distance outside the triangle formed by the three outer stations. Assuming this core location to be correct, the total particle size of the shower was then calculated as $\sim 2 \times 10^{12}$ particles.

The accuracy of the core location, well outside the array, must come under some suspicion. Moreover, the detailed distribution of particle density across the small array for this event which was presented by Suga and colleagues at the Twelfth International Conference on Cosmic Rays, Hobart, 1971 (not included in the conference proceedings) shows large fluctuations between neighbouring stations and cannot strictly be called uniform. Furthermore, the muon densities as measured by the underground detectors might indicate that the core is closer to the detectors than is claimed.

There is, however, no question that this is one of the largest showers ever recorded. Even ignoring the density measured at the detectors of the small array, the primary particle must be assigned an energy greater than 10^{20} eV independent of the location of the core. This shower must therefore be added to the increasing number of cosmic ray primaries observed with energy $\gtrsim 10^{20}$ eV. This is in apparent contradiction to the predicted cutoff in the energy spectrum of cosmic rays at $\sim 5 \times 10^{19}$ eV due to interaction with the universal 3 K microwave radiation. The explanation might be that these very high energy cosmic rays are produced fairly locally, and it is interesting that the Haverah Park group point out that one of their highest energy events also comes from the general direction of a pulsar, PSR 2218+47 (D. Andrews *et al.*, *loc. cit.*). The total number of very large events is still rather small, however, and they give no evidence for a preferred galactic source. Only when more events have been recorded will it be possible to say whether or not the highest energy cosmic ray particles arrive preferentially from the centre of the galaxy and to comment on probable sources.—From a correspondent.

Complex Hydrates in the Lower Ionosphere

ON the basis of a model proposed by Nicolet and Aikin (*J. Geophys. Res.*, **65**, 1469; 1960) it was expected that under normal conditions NO^+ and O_2^+ would be the dominant ions in the D region of the ionosphere, extending from about 60 to 95 km. Measurements with a rocket-borne mass-spectrometer by Narcisi and Bailey (*J. Geophys. Res.*, **70**, 3687; 1965) of the Air Force Cambridge Research Laboratories confirmed that these were the major ions above about 83 km, with metallic ions also being present. But they reported that at lower heights the predominant ions were H_3O^+ and H_5O_2^+ . For several years there was some doubt whether these were ambient ions or the products of rocket contamination. The reproducibility of the observations during rocket ascent and descent on this and several subsequent flights have, however, confirmed their ambient nature. In the meantime, similar mass-spectrometry observations have been made by groups at the Max-Planck Institute for Nuclear Physics and the Goddard Space Flight Center.

A significant feature of all these observations is that under normal ionospheric conditions the water cluster ions disappear at a sharply defined level between 82 and 85 km above which NO^+ and O_2^+ are dominant. This sudden change in ion composition is thought to be associated with the marked gradient in electron concentration often observed in the same height range (Reid, *J. Geophys. Res.*, **75**, 2551; 1970). The notion is that the change from the water cluster ions to NO^+ and O_2^+ is accompanied by a decrease in electron loss for, as Professor Biondi and his associates at the University of Pittsburgh have shown, the recombination with electrons of such cluster ions is more rapid than that of NO^+ or O_2^+ .

In this issue of *Nature* (page 215) Johannesen *et al.* describe a study of this transition region based on rocket observations of positive-ion composition, electron concentration, total positive- and negative-ion concentrations and energetic precipitated particles. The rocket was launched about an hour after noon during August 1971 at Andoya, on the east coast of Norway, the intention being to study conditions during the cold summer mesosphere; measurements of the intensity of solar Lyman- α radiation as a function of height made on the same rocket were interpreted in terms of absorption by molecular oxygen to yield the height variation of atmospheric temperature. A particular feature of the mass-spectrometry experimenta was the relatively large mass range covered, 10–140 a.m.u., care having been taken to ensure sufficient sensitivity at the higher masses.

The observations indicate that water cluster ions, $\text{H}^+(\text{H}_2\text{O})_n$, dominated the ion composition below 84 km on both ascent and descent. Furthermore, cluster ions of higher order mass were seen to increase with height until an abrupt change occurred between 84.5 and 86 km, at which height NO^+ , O_2^+ and metal ions became predominant. The observation of the higher order cluster ions $\text{H}^+(\text{H}_2\text{O})_3$, $\text{H}^+(\text{H}_2\text{O})_4$, $\text{H}^+(\text{H}_2\text{O})_5$ and $\text{H}^+(\text{H}_2\text{O})_6$ is an important aspect of the results because it has been considered that perhaps these are the truly ambient ions, their fragmentation during the rocket sampling process giving rise to the lower order ions which are usually recorded. It is, perhaps, of interest to enquire whether the low mesospheric temperatures existing at the time of the flight

render the weakly-bound cluster ions more stable.

During the period of the rocket flight the production of ion pairs was dominated by particle precipitation. The production rate showed little change in the height range in which the composition change was observed but the electron concentration and positive-ion concentration each showed an order of magnitude increase in this same height range. These results taken together indicate a sudden drop in the effective recombination rate where the cluster ions disappear, as expected from previous studies. But the more continuous measurements of electron concentration and positive-ion concentration show that this drop occurs in a height range of only 200–300 m, implying that the change in ion composition also occurs in such a small range of height.

The formation of these water cluster ions from ions produced during or following the primary ionization processes poses a major problem in the D-region. A rapid sequence of reactions beginning with O_2^+ has been found from laboratory measurements but with a recent revision in the production rate of O_2^+ this sequence is now thought to be inadequate below 75 km (Ferguson, *Rev. Geophys.*, **9**, 997; 1971). It is expected that a much more rapid production of NO^+ occurs, and considerable attention is being given to the possible role of this ion as a precursor of the cluster ions. The degree of hydration of NO^+ ions is a chief consideration in these studies and the observation by Johannesen *et al.* of ion masses attributed to the first and second hydrates will be noted with interest. The height variation of atmospheric temperature presented by Johannesen *et al.* shows no evidence of a discontinuity in the height range in which the water cluster ions disappear. It seems likely that their disappearance is associated with the onset of a reaction which interrupts the formation of the cluster ions (Ferguson, *loc. cit.*) rather than a temperature effect.—L. T.

Regge Theory and the ISR

NEW measurements being carried out on the Intersecting Storage Rings (ISR) at CERN to try to determine the precise shape of the diffraction peak in proton-proton scattering at ultra-high energies seem to promise surprising and intriguing results. If the proton can be thought of as an object with some definite size λ , then, according to classical diffraction theory, one would expect the width, Γ , of the diffraction peak (measured not in angle but as a width in the square of the momentum transfer) to remain constant as one goes to higher and higher collision energies, with $\Gamma \propto 1/\gamma^2$. On the other hand, perhaps the most startling result of Regge pole theory is the prediction that the diffraction peak should shrink with increasing collision energy. More precisely, one expects $\Gamma \propto 1/(\alpha' \log E)$. Here α' , the slope of the dominant Regge trajectory, is a fixed number, and E is the total energy in the centre-of-mass. Interpreted in classical terms, this means that the size of the proton increases with energy. This radical picture appeared to be substantiated by experiments done at CERN and Brookhaven some years ago, using protons with laboratory energies from 15 to 30 GeV, corresponding to $E \approx 5.5$ to 7.7 GeV, and by

later experiments at Serpukhov with laboratory energies up to 70 GeV, that is, $E \approx 11.7$ GeV.

With the completion last year of the CERN Intersecting Storage Rings, in which beams of protons moving in opposite directions, each with laboratory energy as high as 26 GeV, collide head-on, it became possible to explore collisions between protons in a new region of ultra-high energy up to $E \approx 52$ GeV. (This would correspond, in a conventional accelerator, to projectiles with laboratory energy of about 1,400 GeV.)

First results were presented at the Amsterdam conference in July 1971 by two groups—the CERN–Rome and the Aachen–CERN–Genoa–Harvard–Torino collaborations. The results contained two surprises. First, the groups differed significantly in their measured values for the width Γ . Second, the measured widths were considerably larger than expected from an extrapolation of the Regge form $\Gamma \propto 1/(\alpha' \log E)$ that had appeared to be well substantiated at lower energies. In fact, Γ seemed to be roughly constant for the range of ISR energies used. The problem of the disagreement between the two experimental groups now seems to be understood. The measurements had been carried out at somewhat different values of the momentum transfer and the width deduced on the very reasonable assumption of a smooth exponential shape for the differential cross-section. The disagreement thus implied either an experimental error or, what is totally unexpected from a theoretical point of view, some non-smooth structure in the shape of the differential cross-section.

Preliminary, unpublished results of a very careful study of the latter shape now confirm that there is indeed a sharp break in the differential cross-section at a value of the square of the momentum transfer ≈ 0.09 (GeV)². As structure in angular distributions is presumably connected with the physical structure of the particle, physicists are faced with a new and unexpected manifestation of some kind of sub-structure in the proton.

These preliminary results also confirm the failure of the simple Regge pole prediction for Γ . It will undoubtedly prove possible to construct a more complicated Regge-type model, involving several poles and Regge cuts, which will fit the data, but that is likely to be an extremely artificial construction.

One of the peculiarities of Regge pole theory has always been that the extension of Regge's ideas, from the realm of non-relativistic potential scattering, where they play a natural and beautiful part, to the realm of relativistic scattering, is carried out in a rather forced and unnatural fashion. A recent attempt by M. Pennington and E. Leader to set up a more "natural" version of a relativistic Regge-type theory led to the remarkable prediction that Γ would decrease with energy in such a way as to simulate the Regge pole behaviour in the "old" high energy region, but would then settle down to a constant value at ultra-high energies (*Phys. Rev. Lett.*, **27**, 1325; 1971). Although the energy variation seems to be roughly correct, the actual value predicted for Γ differs from the measured value at ISR energies by about 15 per cent.

In summary, then, the opening up of a new ultra-high energy region in elementary particle physics has rapidly produced unexpected and puzzling phenomena. The region of "asymptopia", where nature has settled down to a smooth, uninteresting behaviour, with no surprises, may be much further away than many physicists imagined.—E. L.

Masked Messengers

BEFORE fertilization, sea urchin eggs have only a very low, basal, level of metabolic activity. After fertilization, however, the whole programme of early development is set into motion; protein synthesis increases rapidly, polyribosomes become detectable in cell extracts and RNA starts to be transcribed off DNA templates. DNA replication and cell division also take place approximately once every 40 minutes, so that by 6 hours the embryo is a blastula of about a thousand cells, actively swimming around by means of cilia on its outer surface.

Although the whole of this early development is strictly dependent on the continued synthesis of protein, surprisingly little of it seems to require proteins coded for by messenger RNAs transcribed in the first few hours after fertilization. If more than 90 per cent of new RNA synthesis is inhibited by incubating embryos in actinomycin D they will nevertheless develop, albeit more slowly than normal, into ciliated, swimming blastulae (but no further). Moreover, if sea urchin eggs are gently centrifuged so that the heavy, yolk-filled halves are split away from the lighter, nucleated segments, the enucleated halves will still show a large increase in protein synthesis and polyribosome content following parthenogenetic activation.

These, and other more indirect observations, led to the idea that messenger RNAs for certain proteins needed during very early development are laid down in the egg cytoplasm during oogenesis, and are not translated until after fertilization. These mRNAs became known as "maternal" or "masked" RNAs, but although there is very good evidence for their existence, nearly everything else about them, including their location within the egg, the reason why their translation is restricted before fertilization and the identity of the proteins for which they code, has remained elusive.

Recently, however, work from Paul Gross's laboratory in the Massachusetts Institute of Technology has suggested that at least some of these maternal messages code for microtubule proteins, or, more correctly, for soluble proteins which, after partial purification by vinblastine precipitation, co-migrate on acrylamide gel electrophoresis with known microtubule proteins from sperm tails (Raff *et al.*, *J. Cell Biol.*, **50**, 516; 1971). Although there is a pool of these microtubule proteins in the unfertilized egg it seems that this pool is maintained or supplemented by continuous synthesis of the monomeric subunits, starting from the very first cleavage cycle. It is proposed that during development subunits may be withdrawn from this pool for constructing, among other things, transient mitotic spindles or the more permanent cilia.

The first hint that the new microtubule proteins might be synthesized upon stored templates came from the observation that radioactive amino-acids were incorporated into these proteins even by embryos cultured in the presence of high doses of actinomycin D. On page 211 of this week's issue of *Nature*, the MIT group further substantiate their claim by reporting experiments designed to eliminate alternative explanations for this phenomenon. For example, they show that the radioactive labelling of the microtubule proteins is a result of true protein synthesis and not of the end-addition of amino-acids. They also eliminate the possibility that the relevant mRNAs are particularly resistant to actinomycin

D by showing that microtubule proteins are still synthesized in parthenogenetically activated, nucleated half-eggs. Finally, the fact that microtubule synthesis occurs in eggs preincubated and fertilized in high doses of actinomycin D and ethidium bromide makes it very unlikely that the mRNAs are transcribed from mitochondrial DNA.

This additional evidence is very encouraging and leads one to hope that the identification of specific proteins coded for by maternal mRNA will make it easier to answer some of the other intriguing questions about "masked" messages — for example, whether, before fertilization, they are encapsulated in structural proteins or special membranes, or are protected from translation by the binding of specific repressors or by the presence of polynucleotide sequences that are later removed. There are also several alternative mechanisms for "unmasking" the mRNAs; they could be released at random after fertilization or there could be a programmed recruitment of the inactive mRNAs on to the ribosomes. Finally, it should be mentioned here that there is now quite good evidence against the completely different hypothesis that all the maternal mRNAs are, in fact, freely available for translation, but the ribosomes only gradually acquire the ability to load on to the messenger molecules after fertilization. This model predicts an increase in the size of functioning polyribosomes during the critical 2–3 hours after fertilization, when there is the largest increase in the number of polyribosomes and the rate of protein synthesis. But a detailed study (Humphries, *Dev. Biol.*, **26**, 201; 1971) failed to show any significant change in polyribosome size during this period, thus favouring the alternative hypothesis of the gradual release of "masked" messages, which are immediately fully loaded with ribosomes.—B. H.

PEAT

Erosion in the Pennines

from a Correspondent

VAST tracts of bleak peatlands deeply dissected by erosion gullies are a familiar sight to anybody who travels across the southern Pennines or in the uplands of mid-Wales. Yet in spite of the conspicuousness of upland peat erosion as well as its possible economic importance, especially in water catchment areas, very little work has been carried out on the mechanisms and consequences of the process of erosion. Early work by Bower, Conway and more recent researches by Crisp and Tallis leave a number of important questions unanswered. What are the agents which induce peat erosion? Is



it a physical or a biological process? Does the rate of erosion vary from season to season and from year to year? How old are these erosion channels and could their development be associated with human activity, either directly by way of air pollution or indirectly through sheep grazing?

Answers to some of these questions were provided by Dr J. H. Tallis (University of Manchester) at a joint meeting of the Mires Research Group and the International Peat Society held at the Botany Department of King's College, London, on January 10. Dr Tallis presented some preliminary results of a detailed study which he has been making of a single erosion gully in Featherbed Moss in the South Pennines. By trapping and collecting suspended peat in the water passing down the gully, he has been able to determine rates of erosion at various times of the year and to correlate these with various climatic parameters.

The greatest erosion seems to occur during winter months especially when frost has broken up the surface of the peat and is followed by snow-melt resulting in excessive water runoff. It may be that the erosion which does occur in summer months is simply the residuum of the frost-shattered scree of peat which has accumulated during the winter. The alternative causative agent—drying of peat associated with wind erosion—was dismissed by Dr Tallis as being of little significance except possibly in late summer. Dr Tallis stressed the correlation of high erosion rates with high water flow rates in the gully, caused either by snow-melt or by storms. For the gully in question, flow rates of less than 40–50 litres per minute were associated with negligible losses of peat, whereas the high rates (up to 400 l./min) which he recorded were correlated with very high levels of suspended peat. The total

peat lost from the gully in a year amounted to between 150 and 250 kg. By estimating the total volume of his gully Dr Tallis calculated that it must have taken 200–300 years to form, assuming a constant annual erosion rate.

Pollen analyses and radiocarbon dating determinations have also been carried out in erosion areas and these tend to confirm that the bulk of peat erosion in the southern Pennines is fairly recent in origin. There remains the problem of what initiates the instability which leads to frost shattering and gully erosion. Changes have presumably occurred in the surface crust of vegetation, but are these changes an inevitable climax to the biological succession involved in blanket peat formation, or have they been induced by extrinsic environmental change, be it climatic or anthropogenic? For the time being this question must remain unanswered.

MUSCLE

Innervation in Culture

from our Neurochemistry Correspondent

TISSUE culture, the classical technique of developmental biologists, presents certain advantages to students of the nervous system interested in the formation and specificity of neural connexions. By allowing the observation of homogeneous populations of cells in a controlled chemical environment it avoids the problems of complexity and relative inaccessibility which commonly obscure experimental approaches to the nervous system. A recent article by M. Kano and Y. Shimada, of Chiba University, Japan (*J. Cell Physiol.*, **78**, 233; 1971), demonstrates a relation between innervation of muscles in culture and restriction of their sensitivity to acetylcholine and suggests that this approach may be successful in examin-

ing more widely the nature of neural influences during the development of synapses.

Synapses newly formed in culture between spatially separated explants of chick muscle and spinal cord were first demonstrated, morphologically, by James and Tresman in 1968 (*Nature*, **220**, 384). Cultures of chick embryonic muscle, previously dissociated into individual cells by mild trypsin digestion, have since been shown by several workers to form neuromuscular synapses capable of transmitting impulses when grown with fragments of spinal cord or similarly separated spinal neurones. At mature neuromuscular junctions, transmission normally occurs by the release from the nerve terminal, in response to the arrival of nerve impulses, of discrete quantities of a chemical mediator, acetylcholine (ACh), which acts with receptors at the specialized "end-plate" sites on the muscle membrane causing a fall in the membrane potential (called the "end-plate potential" or e.p.p.), which triggers activity in the muscle. Release of ACh at a low level occurs continuously and gives rise to small fluctuations in the muscle membrane potential, known as miniature end-plate potentials, or m.e.p.p.s, but the rate of release of ACh packets is vastly increased by activity in the nerve terminals, such that the m.e.p.p.s summate to produce potential changes large enough to excite the muscle.

Microelectrode insertions into cultured chick muscle fragments or myoblasts have revealed both m.e.p.p.s, occurring spontaneously, and e.p.p.s, in response to electrical stimulation of spinal cord fragments or nerve fibres, soon after the formation of nerve-muscle contacts, and in some cases even before the muscles themselves were capable of contracting (Robbins and Yonezawa, *Science*, **172**, 395; 1971). These potentials could be blocked by *d*-tubocurarine, a well-known antagonist to ACh at the receptors of the mature neuromuscular junction. This suggests that the potentials were caused by release of ACh by a process similar to that occurring *in vivo* during normal neuromuscular transmission.

Adult skeletal muscle fibres are normally sensitive to ACh only at the small end-plate regions where contact is established with nerve endings. But if a muscle is deprived of its nerve supply it becomes responsive to ACh along the entire length of its surface. Conversely, if the motor nerve fibres are allowed to regenerate into a denervated muscle, the sensitive area shrinks progressively and becomes restricted to the junctional region. Similarly, foetal muscle fibres are uniformly sensitive to ACh, but after birth there is a retraction of sensitivity, this occurring in parallel with

the development of the characteristic end-plate structure.

In the experiments of Kano and Shimada, the ACh sensitivity of muscle fibres grown in culture from initially dissociated myoblasts was tested by iontophoretic application together with intracellular recording. It was found that, like foetal and denervated muscle, cultured fibres grown in the absence of neural tissue gave responses to ACh along their entire length, but fibres grown in the presence of spinal cord fragments, and which showed morphological evidence of nerve-muscle contacts, were sensitive to ACh only at those regions of contact.

This suggests that neuromuscular connexions developed *in vitro* are similar to those of the adult animal not only in respect of transmission of impulses, but also in respect of restriction of chemosensitivity.

The nature of the influence causing

this selection process is still controversial. Contact with nerve endings seems to be essential, but this could provide a number of possible factors. It was originally suggested that there might be release of some chemical from the nerve endings, loosely called a "trophic substance", but to date no such substance has been successfully identified. It is possible that ACh itself may be the elusive factor, but recent experiments have suggested that it might be impulse activity in nerve endings, and hence in muscles, which is critical in restricting sensitivity, because, in animals in which conduction of impulses in particular motor nerve terminals was blocked with a local anaesthetic, but in which the corresponding neuromuscular junctions remained structurally and functionally intact, the entire surface of the muscle fibres involved became sensitive to applied ACh (Lømo and Rosenthal, *J. Physiol.*, **216**, 52P; 1971).

Genetics of Immunological Responsiveness

THE capacity to make an immune response is affected by several basic variables such as the nature of the responding organism, and the quantity, quality and route of introduction of the antigen. Aside from the phylogenetic studies, which have revealed variation between species in the capacity to respond to particular antigens, great interest has developed in recent years in the discontinuous variation in immunological responsiveness which can be revealed within species. Genetic studies of responsiveness have appeared and there has been much talk of "responders" and "non-responders". One hope from these studies is that more information will accrue about the nature of the immune response by elucidation of its mode of genetic determination. The genetic basis of susceptibility to disease may also be clarified. Gasser and Schreffler, in next Wednesday's *Nature New Biology* (February 2), present a study on the effect that the *H-2* locus can have in mice on the capacity to respond to Ea-1 antigens.

In his earlier studies, Gasser has shown that CBA and BALB/c mice are incapable of producing an immune response to the Ea-1 antigens which are present on the erythrocytes of certain wild mice but which are not, as far as can be determined, found in either BALB/c or CBA mice. In contrast, most YBR mice do respond. Responsiveness for an individual mouse seems to be an all-or-nothing response. All the strains involved in the test are inbred and therefore presumed to be genetically homogeneous. Crosses of YBR and CBA mice revealed that responsiveness was a recessive characteristic which further studies showed was controlled by a single Mendelian gene

designated *Ir-2*. The failure of some YBR mice to respond was not adequately explained but was thought to be related to non-genetic factors. Gasser went on to show that the responder trait behaved as a dominant characteristic in crosses between YBR and C57Bl/10 (B10) mice. But further crosses between the F1 animals and backcrosses to the parental generations indicated that a single gene hypothesis could not account for the results obtained. Two-way selection experiments (breeding from responders or non-responders) successfully produced high and low responding lines establishing without doubt that genetic factors were, however, involved.

In their latest article Gasser and Schreffler have continued by typing the animals in the F2 generation of the cross between YBR and B10 for their *H-2* histocompatibility antigens. There was found a significant association between the responsive trait and those animals which carried the *H-2^a* allele. Gasser and Schreffler then repeated the cross between YBR and B10 but used this time a congenic variant B10 D2 which has the *H-2^a* allele rather than *H-2^b*. The results were clear-cut and indicated that the *Ir-2* gene segregated in the expected manner when the *H-2^a* gene was homozygous throughout (the YBR strain is itself *H-2^a*).

These results, aside from the interest of the finding that the *H-2* locus can have an effect on immunological responsiveness, also hint at the possibility that apparently complex modes of inheritance of responder traits may on analysis prove to have single gene bases, the expression of which is susceptible to modification by the products of other gene loci.

MEDICAL RESEARCH

Oncogenesis Debated

from a Correspondent

IN the lecture theatre of the British Museum (Natural History), some years ago, was held a symposium on aggression at which the audience was told that ritualization is a device adopted by many living species for keeping arguments within reasonable bounds. At the same venue on January 17, an audience was treated to an example of ritualized aggression between Dr J. F. Watkins (Sir William Dunn School of Pathology, Oxford) and Professor Sir David Smithers (Royal Marsden Hospital, London) during the second meeting in the series on principles of experimental and clinical oncology organized by the Institute of Cancer Research (see *Nature*, 235, 129; 1972). Sir Oliver Scott was the referee. The aim was to dissect the roles of cell and environment in oncogenesis. Dr Watkins felt that understanding at the molecular level could form the basis of a cure. His presentation rested on an analytical approach to the nature of malignant change largely carried out *in vitro*. Sir David, with thirty-six years of clinical experience, considered that cancer is an organizational defect.

Dr Watkins first distinguished between growth control and topological control. Different degrees of each were named, by reference to the terminology of bacterial genetics, stringent and relaxed. For full malignancy, Dr Watkins envisaged that topological and growth control mechanisms are relaxed. Benign tumours were thought to have lost growth control but to be contained by their surroundings and thus still sensitive to topological controls.

The early *in vitro* studies by Sanford and Earle had established that a change to a malignant condition could occur *in vitro* though, of course, the change could only be proved by implantation to a living animal. But the defect of these studies and later work using chemical carcinogens was the uncertain time lapse between the application of the stimulus to change and the change itself. Dr Watkins felt that carcinogenesis by viruses *in vitro* did not suffer from this drawback and he devoted the rest of his talk to this topic. He excluded RNA viruses from consideration. Part of the difficulty, Dr Watkins said, was that it was impossible to establish a perfect correlation between malignant change and some feature of cells *in vitro* such as morphological transformation, loss of contact inhibition or agglutinability by the wheat germ lectin. For example, it seemed that reversion to a non-malignant condition could occur in tissue culture with

SV 40 transformed cells of a mouse embryo strain. Although contact inhibition was regained, however, the capacity to form a tumour in an appropriate host was more sporadic. Perhaps the delineation of what is a suitable host is the weak link here.

Dr Watkins turned to consider whether malignancy could be attributed to an oncogene (following Huebner). In outline, he said it was an easy question to answer—simply hybridize malignant and non-malignant cells and determine whether the resulting heterokaryons could grow in an immunologically suppressed host. The story is complicated, however, by the finding that the result obtained depends on the number of chromosomes lost from the hybrid cells. The results could, overall, be said to support either a deletion or recessive mutational hypothesis, but until there developed some means for cloning hybrid cells without loss of chromosomal material no definitive answers would emerge. Dr Watkins final conclusion was that one should learn about the molecular basis of malignant change but that the learning would involve a slow collection with "heat and acrimony" of many apparently disconnected facts.

As a clinician, Sir David Smithers had collected a different set of criteria for malignant cell populations. The things that impressed him were the many predisposing factors, the long latency, multicentric origins, increasing autonomy, that site frequency was related to the growth characteristics of a tissue or organ and that tumour cell populations were heterogeneous. Of secondary interest were the tendency to metaplasia, conditional persistence, hormone dependency, maturation and spontaneous regression. Of these factors, he felt hormone dependence was the most significant discovery. Sir David, quoting his elders, tried to establish that cancer should be thought of as a distortion of normal tissue rather than a distinct qualitative change. Furthermore, he insisted that cancer should be described in relation to the whole organism.

NEONATES

Breast Milk and *E. coli*

from a Correspondent

GASTROENTERITIS is often considered to be a mild disorder, but in babies in the first few weeks of life it can be lethal. Paediatricians are thus most interested in the observation that breast-fed babies are less at risk. The greater problems of hygiene involved in bottle-feeding a baby seem not to be the whole story, and it is important to know the factor in breast milk that increases the resistance to gastroenteritis.

It is the multiplication of bacteria, most usually certain forms of *Escherichia coli*, that can exist harmlessly in the bowel in small numbers that causes gastroenteritis, and this increase is less common when babies are breast-fed. *E. coli* reproduces more slowly in an acid environment, such as is produced in the bowel by a harmless bacteria *Lactobacillus bifidus*; these bacteria are more plentiful in the intestines of breast-fed babies.

But it now seems that this may not be the only mechanism involved in the disorder. J. J. Bullen, H. J. Rogers of the National Institute for Medical Research, Mill Hill, and L. Leigh of the Rowett Research Institute, Aberdeen, have shown that human milk can have a specific inhibitory effect on *E. coli*. They attribute this effect to the action of an iron-binding protein—lactoferrin, and possibly the related substance transferrin—in combination with a specific antibody to *E. coli* which stops its multiplication (*Brit. Med. J.*, 1, 69; 1972).

In experiments *in vitro* under conditions of controlled pH, Bullen, Rogers and Leigh found that lactoferrin alone added to *E. coli* reduced the viable count to one fiftieth of the control, and the addition of *E. coli* antiserum slightly reduced the viable count. Used together, however, there was a pronounced effect in which the viable count was reduced to about one three-thousandth of the control. Human milk gave comparable results in the same series of experiments. It seems to be the iron-binding properties of lactoferrin which are significant, for Bullen, Rogers and Leigh found that the saturation of lactoferrin with iron negated the inhibitory effect. Why this should be so is not at all clear.

So how are the two possible mechanisms for inhibiting *E. coli* related? Bullen, Rogers and Leigh investigated this point by experiments in guinea-pigs, whose milk for these purposes resembles human milk. What seems to happen is that the inhibitory effect of lactoferrin with specific antisera operates to keep down *E. coli* for the first few days after birth until the bowel has been well colonized with *Lactobacilli*.

By clarifying the mechanisms by which breast-feeding confers resistance to gastroenteritis, this work will give further substance to the argument that breast-feeding is in general better than artificial feeding. Cow's milk contains less lactoferrin than human milk, and although the amount of transferrin is greater, it may well be denatured by the processing that makes the milk digestible. Furthermore, the addition of iron to cow's milk to bring the iron content up to the level found in human milk probably saturates the remaining lactoferrin and transferrin.

GRAVITATIONAL RADIATION

Too Much Too Soon?

by our Cosmology Correspondent

THE specialist discussion held at the Royal Astronomical Society on January 14 may be remembered as a historic occasion. This was the first time that the society has devoted a meeting to the subject of gravitational waves; but if the experiments now being designed and built around the world to test Weber's claims result in the unequivocal identification of these waves there will certainly be many more meetings to discuss them.

Gravitational wave astronomy has had a chequered history. For many years it seemed clear from any conventional understanding of astronomical processes and general relativity that the chances of detecting such waves on Earth were so small that it was not worth looking for them. In the face of this understanding Professor Weber has built progressively more sophisticated detector systems, and these have certainly detected something. But the number and magnitude of the events detected by Weber suggest that if they are bursts of gravitational waves then matter is being converted into this radiation in our galaxy at a rate which is unbelievable to many astronomers. Clearly, independent observations confirming Weber's results are required, and whatever conventional theories may predict there is now, as a result of Weber's work, a major incentive to develop suitable experiments.

There is no great difficulty today in constructing detectors which will operate at the level of the events recorded by Weber. Mr G. W. Gibbons (University of Cambridge) described these transverse waves, which propagate at the speed of light, and their effect on test particles. The waves produce a shear stress over a plane perpendicular to the plane of propagation of the wave. A circle of test particles in this plane will be repeatedly deformed into an ellipse and back to a circle by this stress, and because of polarization two modes of deformation, at 45° to each other, are possible. Although it is difficult to provide a ring of freely suspended particles which could detect such waves, they will also cause a regular increase and decrease in the separation of any two particles at the ends of a diameter of the ring, or in the length of a bar placed across such a diameter.

Dr P. Aplin (University of Bristol) described Weber's own detectors and others now being built which incorporate this principle. Provided that the changes in length caused by gravitational waves can be measured, a bar oriented east-west on the Earth will be carried round every twenty-four hours

to provide a scan giving some indication of the direction from which the waves are coming. Because of the transverse nature of the waves, they should be detected preferentially at 12-hour intervals, if they have a reasonably localized origin.

The small amount of variation in the length of any experimentally feasible bar makes it impossible to use optical interferometry, perhaps the obvious monitoring technique. Piezoelectric techniques are, however, much more sensitive, and by attaching chips of piezoelectric material to the test bar changes in length caused by thermal oscillation, for example, can be easily detected—that is, changes of $\sim 10^{-14}$ cm. Otherwise, the original equipment used by Weber was dictated chiefly by

requirements that it be simple and relatively easy to construct and operate. Thus, the 5-foot long, 2-foot diameter aluminium bar weighing roughly 1½ tons, which provided the first convincing evidence that gravitational waves might exist, was chosen on grounds of expediency, and not through any belief that its resonant frequency (1,660 MHz) might lie in a region of unusual gravitational wave activity.

The first sign that something unusual was being detected came in 1967. This evidence took the form of a tail to the Gaussian distribution of random noise frequencies in the bar, and encouraged the construction of a second experiment, at first on the same site in Maryland and later moved to Argonne, 1,000 km away. It is the coincidences

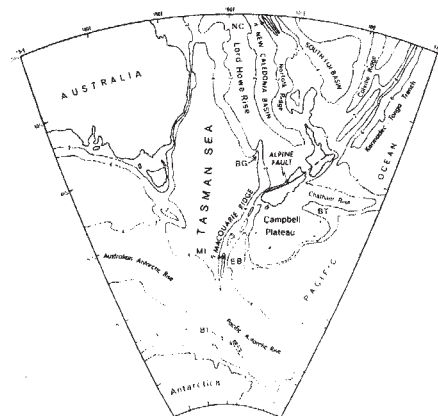
Plate Tectonics of the Tasman Sea

IN next Monday's *Nature Physical Science* (January 31) Griffiths and Varne suggest a two-stage pattern of evolution for the complex region centred on the Tasman Sea which is based on both geological and geophysical evidence. At present the Tasman Sea (see map) is an aseismic region within the Indian-Australian plate but bounded at the south-east by an active margin (the Macquarie Ridge) which separates it from the Pacific plate. To the north it tapers between Australia to the west and the Lord Howe Rise to the east but to the south it opens widely into the Southern Sea. It is an oceanic area with a crust about 5 km thick, and although it has not been surveyed throughout in great detail, it is known to produce some linear magnetic anomalies.

This is the Tasman Sea today—but how has it evolved and what is its relationship to the geological features which surround it? The starting point for the Griffiths-Varne model is the separation of the Campbell Plateau and Antarctica which began about 80 million years ago according to magnetic data. At this time the Tasman Sea began to open as an area of triangular rifting with a northward movement of the apex between Australia and the Lord Howe Rise resulting from an anticlockwise rotation of the Campbell Plateau between 80 and 50 million years ago. About 50 million years ago, however, seafloor spreading also began between Australia and Antarctica, thereby causing a major change in the evolutionary pattern of the whole region.

For the next 40 million years both Australia and the Campbell Plateau moved away from Antarctica but at different rates. Analysis of the magnetic profiles suggests that over this period Australia moved at about 2.0 to

2.5 cm yr⁻¹ relative to the Campbell Plateau thereby producing a relative displacement of about 800–1,000 km which Griffiths and Varne suggest was taken up by the Tasman Sea. Assuming that the continental blocks forming the Campbell Plateau and the Lord Howe Rise have always remained in contact (that is, between 50 and 10 million years ago) and that there has been no appreciable north-south differential slip in the northern Tasman Sea (there is apparently no evidence which invalidates these assumptions), Griffiths and Varne then conclude that the relative motions of the features surrounding the Tasman Sea are only explicable in terms of further spreading in the sea itself. So far, however, the data are not available to enable the spreading to be described in detail although the greater part probably took place in the southern area. Finally, spreading in the Tasman Sea apparently stopped about 10 million years ago when the spreading rates between Australia and Antarctica and between the Campbell Plateau and Antarctica became about equal. At this point the new plate geometry became established.



between events recorded independently by these two experiments that Weber puts forward as proof of the existence of gravitational waves, because there seems to be no other phenomenon which could disturb both bars in the appropriate way at the same time. Unfortunately, however, many astronomers are concerned about the statistical techniques used by Weber in deciding which coincidences are real.

But just why do Weber's claims cause so much concern? The answer is simply that they seem too much of a good thing. Dr M. J. Rees (University of Cambridge) explained just what the observations imply, taken at face value. Weber reports bursts of gravitational waves, coming roughly from the centre of our galaxy at a rate of one or two per day. If this is typical, and the waves are emitted isotropically from the galactic nucleus (some 10 kpc from Earth), then the luminosity of the nucleus in gravitational radiation alone is 10^{51} erg s⁻¹. Although it is now known that in certain circumstances the collision of two black holes can result in the loss of half the total mass of the pair as gravitational waves, the total mass loss from the galaxy implied by this large luminosity is $2 \times 10^4 M_{\odot}$ yr⁻¹. This is the figure on which many astronomers choke, for it implies that the galaxy is losing mass so rapidly that there should be observable effects on the orbits of its constituent stars. These effects are not seen.

There are two ways out of this dilemma. Either Weber is wrong or general relativity is wrong. Each alternative raises interesting possibilities. First, if Weber has not detected gravitational waves, what has he detected? Second, if general relativity can be proved to be wrong in this instance the gates will be opened, once and for all, to those theoreticians who have been claiming for some time that a new theory of gravitation is needed. One suggestion put forward at the meeting is that if matter creation is taking place at the nucleus of our galaxy then gravity waves might be produced in abundance by the same process.

These questions may now be resolved in a matter of months. Throughout the world, many groups are working on the search for gravitational waves, and the first Weber type detector in Britain has just been completed in Glasgow. The Bristol team also have detectors in an advanced stage of construction. A joint Bristol-Glasgow experiment seems particularly desirable, because not only would this have a suitably large baseline to remove spurious effects but also it would have the advantage of two independent teams with no personal axes to grind conducting the tests for genuine coincidences.

CHEMISTRY

Probing the Structure of Acetylacetone

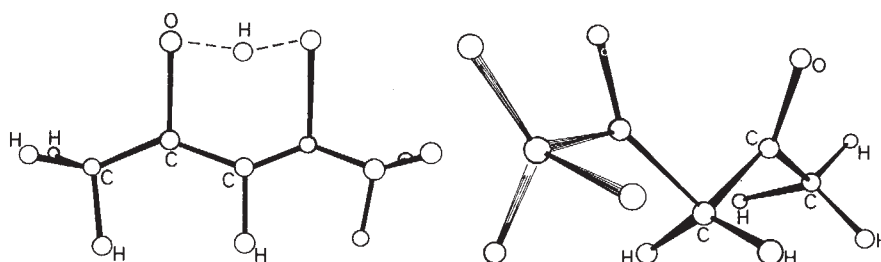


Fig. 1 Structures of enol and keto forms, respectively, of acetylacetone.

ELECTRON diffraction studies of the "enol" form of acetylacetone—the tautomeric species that makes up varying proportions of the compound at different temperatures, 65 per cent at 100° C for example—have revealed that the hydrogen bond between the two oxygen atoms is linear, symmetric and short in the vapour phase.

Although this is not an entirely unexpected result in view of the discovery in 1966 of a similar short bond (2.424 Å) in tetraacetylene, a dimer of acetylacetone, the even smaller value of the OO separation in acetylacetone(enol) of 2.381 Å is somewhat surprising and indicates that the five-membered ring has definite aromatic characteristics.

These structural determinations are

described by Lowrey, George, D'Antonio and Karle (*J. Amer. Chem. Soc.*, **93**, 6399; 1971). Fig. 1 shows, approximately to scale, the structures deduced by Lowrey *et al.* for both the keto and enol forms. The OO bond length of the keto form is 2.767 Å.

Acetylacetone is important because of its ability to undergo the chelation process, forming heterocyclic rings containing at least one metal cation or one hydrogen ion (as in the enol form). The metal chelate ring compound of the enol form of acetylacetone contains very stable six-membered rings, and the overall stability is reflected in the fact that beryllium acetylacetonate, Be(acac)₂, boils without decomposition at 270° C.

Silicate Liquid Immiscibility

ALTHOUGH molten rock erupted at the surface and intruded into the Earth's crust is essentially a silicate melt, it displays wide variations in its chemistry, the elucidation of which has long taxed the ingenuity of petrologists. By far the most popular explanation is that most igneous rocks start as low-silica, high-magnesia melts in the Earth's mantle, which are then modified on their way to the surface by processes of crystallization or contamination. Another possibility is that primitive melts might separate on cooling into two or more immiscible liquids, to provide a range of lava compositions. The few adherents to this idea had previously to contend with abundant experimental evidence against liquid immiscibility in those silicate melts which correspond to common rock compositions. Evidence of liquid immiscibility in the glassy parts of the lunar samples from Apollo 11, however, has undoubtedly helped to stimulate renewed interest in terrestrial examples, as witnessed in recent geological literature (see, for example, *Nature*, **229**, 107; 1971).

In next Monday's *Nature Physical Science* (January 31) another example of immiscibility is claimed by J. Ferguson and K. L. Currie to be present

in some of the oldest volcanic rocks of the Earth's crust, the Swaziland Sequence of southern Africa. Some of the dark basaltic lavas contain pale globules up to 10 cm in diameter which, the authors argue, formed as immiscible drops from an originally homogeneous liquid as it was cooled. Melting experiments on these lavas show signs of liquid unmixing between 1,100° and 1,200° C.

Analysis of the two components of the globular rocks shows a spread of composition that could explain part of the total chemical range of the Swaziland lavas: Ferguson and Currie deduce that liquid unmixing was an important factor in producing this range of compositions. The ancient Swaziland rocks are now wholly crystalline and, moreover, have suffered mineralogical alteration; some petrologists will argue that, consequently, their precise liquid compositions are unknown and that the phase structure cannot be accurately recreated.

Many other questions will be raised by Ferguson and Currie's conclusion, not least of which will be the long-standing fundamental problem of how two silicate liquids could be cleanly separated to produce distinct eruptions.

ENZYMES

Pursuing Pyridoxal

from our Molecular Biology Correspondent

PYRIDOXAL phosphate is an accessory built into a variety of enzymes, and in many cases its direct participation in the catalytic process can be inferred with some confidence. The pyridoxal is attached to the protein by way of a Schiff base linkage to a lysine side chain, and therefore serves as an irreversibly bound label if the aldamine group is first reduced with borohydride. Several groups of workers have been exercised to discover whether there are underlying structural and functional similarities between different enzymes having this one feature in common. The isolation and sequence determination of tracts of residues around the phosphopyridoxyllysine in three further enzymes now invites a search for generalizations.

A brace of articles, one by Fluri, Jackson, Lee and Crawford (*J. Biol. Chem.*, **246**, 6620, 1971), the other by Maurer and Crawford (*ibid.*, 6625), give the sequences of pyridoxal-containing fragments of twenty-three residues from the tryptophan synthetase β subunits of two different bacterial species. Tryptophan synthetase is a tetramer containing chains of two kinds, α and β , each responsible for a partial synthetase reaction, and the pyridoxal phosphate is present in the second. The identification of the two tryptic peptides containing the prosthetic group is facilitated by the use of tritiated sodium borohydride for the reduction before proteolysis. The appearance of two pyridoxal peptides in both cases is a curious feature but evidently does not reflect any heterogeneity in the protein: a difference between the two peptides of a terminal arginine and the presence of arginine in the digests indicate rather that scission occurs on either side of an arg-arg or lys-arg pair. At all events, the enzymes from both *Escherichia coli* and from a pseudomonad each yield a unique peptide sequence with the pyridoxyllysine near the middle. In spite of large differences between the two proteins, in respect of total peptide maps, which are unrelated, immunological reactivity, and failure to hybridize with one another, the sequences of the fragments are distinctly similar. The three residues to the N-terminal side of the pyridoxyllysine are identical, and indeed fourteen of the twenty-three residues are conserved. Of the rest, the majority of substitutions are conservative, and the number and positions of the charges are completely unchanged. Such a high degree of conservation points to the functional importance of many of the residues in the vicinity of the pyridoxal phosphate.

The pyridoxal peptide sequence in a

quite different bacterial enzyme, arginine decarboxylase of *E. coli*, has also been determined by Boeker, Fischer and Snell (*ibid.*, 6776). The strategy here preferred for the identification of the pyridoxal-containing tryptic and chymotryptic fragment involves a variation on Hartley's diagonal mapping technique. This approach, which has wrought a minor revolution in protein chemistry, consists simply in the chemical modification of the residues of interest directly on the chromatography paper after separation in one dimension, followed by an identical separation in a direction perpendicular to the first. All peptides that are untouched by the treatment therefore appear on the diagonal, and contrariwise, those not lying on the diagonal contain the desired groups. Boeker *et al.*, preferring ion-exchange columns to paper, simply chromatograph aliquots of the peptide mixture on the same column before and after modification—which in this case consists of stripping the negatively charged phosphate from the prosthetic group by exposure to alkaline phosphatase—and collect the components with changed elution characteristics. They give the sequence of a pyridoxal-containing peptide of seventeen residues, which may now be compared with those of the eight other pyridoxal enzymes that have been studied.

Closest to the arginine decarboxylase pyridoxal peptide is that from glutamine decarboxylase of the same organism. Similar as these two enzymes are in function, they are structurally quite

different in terms, for instance, of molecular weights and numbers of subunits. Only eight residues are available for comparison, and of these three are identical, and two represent conservative substitutions. In particular, the nearest neighbour of the modified lysine on the N-terminal side is in both cases a histidine, and this holds good also for the two tryptophan synthetase β -chains. In all these species the mechanism of catalysis is thought to involve the pratonation of a substrate α -carbon in an intermediate state of Schiff base character, and the histidine residue is thus an obvious candidate as a participant in a proton transfer process. The other enzymes available for comparison have unrelated functions, but Boeker *et al.* argue that it might commonly be desirable to stabilize the cofactor attachment by ion-pairing between the phosphate of the pyridoxal phosphate and a close-lying cationic group. In one case the adjacent residue is a lysine, and in another an arginine. Studies on yet other related enzymes are, it seems, in progress.

It is worth remarking that pyridoxal phosphate has found wide application as a specific reagent for labelling reactive amino-groups. Two enzymes for which it turns out for this reason to be a specific inhibitor are glutamate dehydrogenase and phosphoglucose isomerase. In the second it has been shown to generate one pyridoxyllysine per active site by Schnakerz and Noltmann (*Biochemistry*, **10**, 4837; 1971) and in the former (Piskiewicz and Smith, *ibid.*, 4538, 4544) such a reactive lysine has

Visible Solar Features and Interferometry

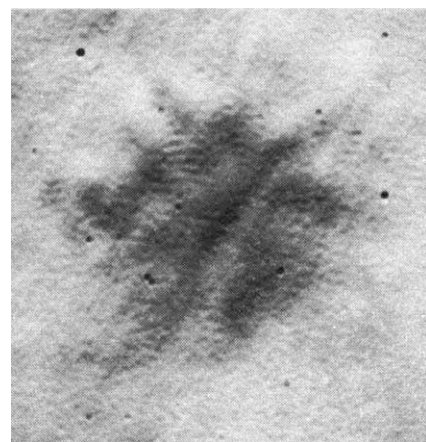
IN next week's *Nature Physical Science* (January 31) J. W. Harvey, of Kitt Peak National Observatory, describes how interferometry (using wave-front division) can, in principle, be used to examine solar features with dimensions of less than 100 km, and to elucidate their structures.

His technique is to cover the entrance aperture of a telescope with a mask containing two rectangular slits, and then to observe the Sun through a narrow passband filter. Photographs taken of a sunspot with this arrangement revealed a fringe system—made much clearer with the help of the filter which reduces the problems associated with dispersion in the Earth's atmosphere—that suggests the existence of small scale features.

The figure here shows a high contrast print of the superposed negative and positive of a single photograph that have been shifted by about half of a fringe period in order to highlight the fringes. The separation of the fringes is about 0.28 arc s, equivalent to about 200 km

or less. Harvey also describes photographs of a larger sunspot which seemed to have features with dimensions as small as 100 km.

The technique, Harvey suggests, may also be useful for the detailed examination of such things as chromospheric structures (such as flares and prominences), faculae and magnetic field elements.



already been identified in the sequence. It is shown that this residue is implicated in the DPNH binding site, and the suggestion is that interaction of the enzyme with pyridoxal phosphate may serve a physiological function.

VIROLOGY

Reovirus Replication

from our Cell Biology Correspondent

REOVIRUS is not oncogenic, it does not contain reverse transcriptase, neither is it, or are its relatives, important pathogens of man or his domestic animals, and yet reovirus continues to attract the attention of many virologists. Why? The chief reason is surely that they cannot resist the fascinating questions that are posed by the curious reovirus genome.

The virus particles comprise an outer protein capsid enclosing a core, an inner capsid within which are ten double stranded RNA molecules, the viral genome. The inner capsid is made of only three species of polypeptide, specified by three of the ten double stranded RNAs, and at least one of these polypeptides apparently acts as a transcriptase synthesizing monocistronic messenger RNA molecules, or plus strands, from each of the ten genomic RNAs.

This transcription, incidentally, occurs efficiently *in vitro* when virus cores are incubated in a suitable incorporation mixture which means that reovirus is likely to prove a useful source of messenger RNAs with which to programme eukaryotic cell-free systems which support protein synthesis. The electron micrographs of Gillies *et al.* (*Science*, **174**, 694; 1971) provide most elegant visual evidence of this transcription and reovirus RNAs have already attracted the attention of RNA chemists; Nichols *et al.*, for example, reported in *Nature New Biology* last Wednesday (**235**, 105; 1972) the sequence of the first twenty-five bases at the 5' termini of some reovirus messengers.

But all that apart, how is the segmented reovirus genome replicated? By analogy with the replication of the single stranded RNA phages one might expect the replication of reovirus RNA to be asynchronous, involving first the synthesis of a single stranded RNA which then acts as a template for the synthesis of its complement, and that is indeed what Schonberg *et al.* recently found (*Proc. US Nat. Acad. Sci.*, **68**, 505; 1971); viral plus strands with the same polarity as viral messengers act as templates for the synthesis of minus strands. Continuing their investigation this group (Acs *et al.*, *J. Virology*, **8**, 685; 1971) now report an analysis of reovirus RNA replication *in vivo* and *in vitro* leading to a speculative model which envisages that the replication of the double

stranded RNAs occurs in nascent progeny virus particles.

The salient observations of Acs *et al.* are, first, that the two strands of reovirus RNA are made *in vivo* and *in vitro* sequentially. *In vivo* plus strands are made early and accumulate such that 8 hours after infection a full complement is available to associate with viral protein. Plus strands made at late times are apparently excluded from this process. The synthesis of minus strands occurs in a cytoplasmic, particulate fraction, the putative nascent virus, that retains its activity after extraction and survives exposure to detergents and chymotrypsin. RNAase added after this particulate fraction had been incubated *in vitro* for 15 minutes had no effect on the amount of double stranded RNA made. By contrast RNAase added at the start of incubation markedly inhibited the accumulation of double stranded RNA.

Two New Protein Structures

THE forthcoming issue of *Nature New Biology* (February 2) contains the results of two X-ray crystallographic studies of protein molecules of great interest. The Uppsala group (Liljas *et al.*) have now brought their work on the structure of human red cell carbonic anhydrase C to a resolution of 2.0 Å, which is sufficient to show the details of geometry at the active site. The molecule overall is an ellipsoid with a deep crevice, at the bottom of which is the active centre. On the surface there are seven short helical segments containing a fifth of all residues. Two of them are true α -helices, and the rest are in greater or lesser degree distorted towards the 3_{10} geometry. On the surface of the molecule, and dividing it in two, is a long segment of β -structure. Perpendicular to its length are short anti-parallel chain segments, which on one side make up a wall of the crevice.

The enzyme contains a zinc atom, which is essential for activity. This is seen to lie at the bottom of the crevice, and to be linked to the protein by three ligands. From the electron density distribution these are identified as histidines. There is a fourth ligand, which is believed to be water or a hydroxyl ion. It is of considerable interest that the coordination is distorted tetrahedral, with a deviation of up to 20°. Two other histidines appear to form a part of the active site. Liljas *et al.* note that in the absence of data on complexes with competitive inhibitors no definite support for proposed catalytic mechanisms can be obtained. It is intended now, however, to proceed to the study of inactive analogues in which the zinc has been exchanged against

Acs *et al.* suggest that once the ribonucleoprotein complex of plus strands and viral protein assemble and minus strand synthesis occurs, other viral proteins condense on the nascent virions rendering them resistant to RNAase. It seems plausible therefore to suggest that the enzyme responsible for minus strand synthesis may be incorporated into the virions. And because reovirus cores contain a transcriptase responsible for the synthesis of single stranded messenger or plus strand RNA it is on the cards that one or more of the three inner capsid polypeptides is a polymerase that can act as a transcriptase or as a double stranded RNA replicase. If these ideas are valid, if the synthesis of double stranded RNA occurs in the nascent progeny particles, there remains the intriguing question of how the plus strands are selected such that each nascent particle contains the one copy of each of the ten species.

other metals, and of complexes with inhibitors.

Poljak and his colleagues at Johns Hopkins University succeeded in crystallizing an antibody fragment, Fab', and now describe the structure at 6 Å resolution. Fab (and Fab' which differs from it by only a few residues) is a proteolytic fragment of immunoglobulin, which contains one of the two light chains and a part of one of the two heavy chains, joined to it by disulphide bonds. Whereas antibodies consist of heterogeneous populations, myeloma proteins are homogeneous, and the preparation used by Poljak *et al.* is of this kind. The Fab fragment carries the antigenic specificity. The light and heavy chains of antibodies are both characterized by a segment of variable sequence, and another which is invariant for a given species.

The electron density maps lead to a picture of the fragment consisting of two globular elements. By tracing the segments of electron density, it is possible to identify one of these with the combined variable parts of the heavy and light chains, and the other with the constant parts of the two chains. This is consistent with known proteolytic cleavage behaviour, and agrees also with inferences from physical measurements. In the globular portion corresponding to the variable chains there is a cleft fashioned from parts of both chains, which is thought to represent the antigen binding site. An overall structure for intact immunoglobulin G involving six globular subunits, two in each Fab piece, and two in the Fc, which joins them roughly in the shape of a Y, is inferred.

An Experiment in Education

HERMAN T. EPSTEIN

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Professor Epstein discusses new approaches to the problems of established teaching methods. He describes a technique of teaching in which research papers are studied in class with a view to finding out what a scientist does and how he works.

SCHOOL structures and teaching methodologies are so primitive at present that almost any education experiment devised by a reasonably intelligent person is bound to succeed. This is not to say that present schooling does not produce many highly motivated and learned persons. The current education turmoil stems chiefly from the greatly increased proportion of youths attending schools and colleges. These additional students simply do not respond to the intellectual fare offered to their more motivated peers. This is an empirical insight, for it was unlikely that society could have predicted their insensitivity to teaching strategies that seemed to work for the intellectual elite. Now that we know that the old ways do not work for most non-academic and non-professional youths, we can seriously suspect that the old ways did not really work for the elite. It was just that motivated students will learn well in spite of almost any structure, any content and any teaching methods. The extent of apparent success of the old ways is to be used as the baseline for measuring the achievements of new ways.

Learning-teaching Process

The most interesting work that I know of is that of the experimenters who have produced Summerhill and the "open classroom". I believe these activities should be judged as experiments performed to learn something about the learning-teaching process (LTP) and not as experiments designed to achieve something. From the point of view of the LTP, these experiments have given both food for thought and data for analysis.

The rationale of my work includes the following principal points. First, no experiment in education should be considered to have produced a worthwhile insight unless it can increase dramatically the fraction of students doing honour work. People who have studied the psychology of learning and the strategies of teaching have produced such minimal results that there is almost no point in paying attention to their theories. The time is overdue for large-scale experiments to arrive at empirically determined ways of setting up schools and the LTP within those schools. It would not be surprising to learn that Ivan Illich is right in asserting that the abolition of most schools would produce more learning by most young people than now takes place within those schools. Second, a significant number of schooling problems arise because most

students are in schools because society demands their presence and in spite of the fact that most students (from the least capable to the most brilliant) find little they want to do in those schools. Third, few detectable changes in college curricula and problems have resulted from the various prestigious high school curriculum reform projects although they are, to most observers, obviously superior to the curricula they replaced. Fourth, the capacities of young minds are so very much greater than they are given credit for by schools today that the chief problem with experimentation is not to concern ourselves about overtaxing the minds of our youth but rather to be audacious enough to try experiments that approach the present limitations of young minds and the LTP. Fifth, the best way to be this audacious is to expose students directly to the latest and most complicated works in any field and to back up (provide background information and outlook) only to the extent needed to let the students get the idea. Sixth, the purpose of an introductory course is to let students learn how significant work is done in the field.

Redesigned Courses

My experimentation began with redesigning the introductory university science course for non-scientists, although since then I have worked on courses for university science students, high school students, high school science teachers and for general adult education.

In the United States there are three principal types of introductory science courses. The first is the time-honoured study of a representative set of the basic laws and theories of the science as currently practised and understood.

The second is the survey course for non-scientists who can be presumed to be taking their terminal course in the science. One wants to give these non-scientists an overview including many concepts and laws that science students reach only in later courses. The increased number of topics *de facto* decreases the study of each topic.

The third type is the case study or general education course introduced by James Conant after the Second World War. This is not a case study in the sense in which the term is used in law schools, business schools and social work schools but rather it is a historical survey of the development of some particular and important concept or law.

I felt that I could discard all three of these types because none had worked so well that it has remained the choice of most colleges. I chose a different goal: I wanted the student to learn what a scientist does when he is working and to learn how worthwhile work is done in the field as well as the ways in which the work can be characterized as worthwhile.

Fundamentally this can be done thoroughly and well only by having students learn the practice of the field as apprentices, much as our graduate students still do. Can this way be approached without introducing great numbers of students into many years of laboratory work in a subject in which they have no primary interest or competence?

The way I chose was to select a set of research papers dealing with the development of one line of research in biology and to have the students study them in a certain way whose nature developed empirically. There is at present no other reading material for this course which takes up 3 hours a week. This is entirely in keeping with the earlier remarks about being audacious enough to bring the students to the frontiers of a science and then to provide only sufficient backing up material to let the students assimilate what they need to understand the frontier work.

The single most important empirical finding about how to study these papers was that the focus of the class discussion must always be on the activities of the scientists who wrote the paper. We continually ask students to put themselves in the places of the experimenters and figure out what to do next and how to do it. This is the orientation of problem-seers and problem-solvers. It is the most difficult capacity to develop in our brainwashed children and it is a capacity that can be and should have been developed in grade school.

Whenever we allowed the focus of discussion to be primarily on the science information itself, we soon lost most of the students. If they were that interested in its experimental informational content, they would be science students. (Indeed, this insight indicates the possible need for modifications of our approach when dealing with students of science.)

Activities and Information

One cannot, of course, talk only about the scientists' activities. Much time is inevitably spent on the information itself. And the students learn an impressive amount of science perhaps because the emphasis is on something else. We utilize this offset of focus by using digressions to insert most of the content of a regular science course.

One could consider, for example, that living organisms all metabolize. Thus, when questions of metabolism arise, one can digress for 5 or 10 minutes to show experimentally how insights into metabolism that permit a grasp of the metabolic point raised in the research paper were gained. During a semester, eight or ten such digressions amount to a substantial study of metabolism. I use the illustration of 5 to 10 minutes because, if digressions lasted more than about 10 minutes, students lost the connexion with the research paper as an activity and began thinking of the information; that ruined the development of their ability to think like researchers. I cannot emphasize too strongly that two or three digressions of 5 to 10 minutes each is the maximum in a 1 hour class period; it is permissible to have fewer. This is an empirical result; it is important to know the result and to utilize it. (This is valid for undergraduates in a university; but digression length and frequency are very different for upperclassmen, for adults and for high school students.)

Most lines of research touch on most of the important functional areas in biology: metabolism, genetics, evolution, growth, and development. Thus, the use of digressions permits a fairly inclusive introductory course to be hung on the hook of learning how to research a particular narrow topic.

The manner of studying the papers is also critical. The instructor refrains as much as possible from explaining almost everything. He must let the students ask questions. He then attempts, in fairly obvious ways, to get the students as a group to figure out how to go about obtaining the answer to a question. The class as a whole eventually arrives at some plausible way of determining the answer experimentally.

In this way the class concentrates on what to do in order to learn something. Initially students do this poorly, if at all, and the instructor gives hints in considerable depth. As the term progresses, the ability to think like a research man is steadily developed. By the end of the term, most students have a considerably increased ability to think like a researcher or, as they frequently put it themselves, they have learned how to think by working on real problems.

It generally takes about 1 month to work through the first paper whether it is one page or forty pages long because the same thing is being done: students are being exposed to the manner of thinking of working scientists, their strategies and tactics and details of the experimental system being studied. Even the digressions to general aspects of biology tend to be rather similar. We have discovered that students begin to tire of the first paper after 3 to 4 weeks.

Choosing the Next Subject

In order to proceed, we then raise the question of what should be done next. With hints, students can propose several different plausible studies in a half hour and instructors are skilled enough to ensure that among them is the subject of the next paper chosen for the class. This process is repeated between each pair of papers so that students have plenty of practice in figuring out the next step in working on a problem.

The second paper generally takes 2 to 3 weeks. Later papers take about 1 week, so that in a semester a class can study six to ten papers.

We have found empirically that students can, by the end of a semester, obtain answers to their important questions which allow them to grasp a substantial part of the research on a level certainly lower than that of graduate students but nevertheless quite impressive to us and satisfactory to them. The better students can handle a paper a day—that is, three a week, with equivalent insight.

Evaluation methods in human affairs are still a subject of the future. In the absence of meaningful and sensitive evaluation methods, I have taken to distributing questionnaires. We tried to reach all graduating students who took our course in 1968–69. Of these forty-five students, thirty-six are still in the university and thirty-two responded to persistent efforts to get the questionnaires filled in. Of these, twenty-one think our course was among the finest they had at the university, four thought it a typical course and seven thought it among the worst courses. Of the latter, six blamed the poor quality on their instructor (and each had had a different instructor!). Yet these six “haters” all thought the format so good that introductory courses in all subjects should be recast into our format. About 80 per cent of all responding students wanted this kind of introductory course in all departments. We also have similar data from other groups that we have contacted. There are, of course, occasional poor instructors and good instructors sometimes have less successful sections. We have now run about forty sections at Brandeis with about thirty different instructors.

Similar results were found at a dozen other universities, chiefly in biology although economics, chemistry and philosophy have had successful trials. The economics version, principally developed at Northeastern University, has been extensively evaluated by giving students examinations set for students in the regular course that used Samuelson's economics text. Interestingly, our special section students do at least as well as those taking the regular course even though the nominal topic of the sections has been as apparently narrow as the use of paramedical personnel in hospitals.

The examinations we have used may be of interest. The most obvious is the “inquiry type” which poses an experimental situation and asks students to plan a plausible experimental attack and deduce the likely results. Somewhat less obvious is the presentation of a short research paper and a request to students to devise the questions and experimentation that might follow up this paper. We have frequently asked students to make up an examination that tests them on the course and then to reply to their own examination. My own favourite is to give students a summary of an existing paper and to ask them to imagine in detail the experiments that must have been done and the results obtained to permit the assertions in the summary.

Another examination scheme has also proved illuminatingly

effective. Students do not sign the examination papers. Their anonymous examinations are commented on frankly and extensively and returned to students who get their own papers because they recognize them. The instructor gets to know the overall progress of the class without being prejudiced by the progress of his subjectively chosen class leaders. Students get a thorough criticism without the associated penalty of having their errors, omissions and misunderstandings counted against them. The popularity of these anonymous examinations has proved that students are entirely willing to undergo intense pressure to study and learn as long as it is not accompanied by the pressure of being graded on the performance. Such examinations are now being set at monthly intervals.

Our failures probably stem chiefly from the fact that published research papers tell only the successful stories and activities; the errors and failures and fumbling around are not recorded. Thus unless the instructors manage to convey the blundering aspect, students miss this frustrating but intriguing part of real scientific activity. I believe that the closer we come to connecting students with the real activity, the greater is the attraction for the students. Thus the investigatory or project laboratory (I-lab) would be the preferred approach if ways could be devised for handling the many students who arrive in American colleges without interest or background in science. So far, in my judgment, the I-labs described by various workers deal with areas and aspects of biology that are far too simple to convey the activities and outlook of modern biologists.

Our instructors teach from papers in their own areas of research expertise and so discussions ring true and students sense this at once. Not all instructors can handle this kind of approach, however. This is not unexpected because we have no panacea. Perhaps the properly modest statement is that we have uncovered a teaching strategy that about one-third of instructors can use well. Hopefully, we are contributing to the awareness that instructors have varying capacities and that each should teach in a way that maximizes his strengths instead of requiring, as is the case in high schools especially, a single approach to the LTP.

During 1969–70, four sections of the course were run at Tel Aviv University for students of microbiology. The response and the effectiveness of the approach were judged to be excellent and the course, given at present for second-year students, will be placed in the first year as soon as scheduling permits. When followed by our version of an I-lab, the combination has proved to be, in the view of the Tel Aviv faculty, an extraordinarily effective way of getting students who are just starting their studies to think and work like scientists.

Adaptation to High Schools

One of the “spin-offs” of this work came from a request to try to adapt the approach for high school students. I did this myself with a class of seniors in a kibbutz high school in Israel. The results were judged to be so favourable that I was asked to try to train high school science teachers to work using this approach. With the help of my Tel Aviv University colleague and friend, Dr Eliora Ron, a training course was improvised that taught the teachers in the way we wanted them to teach their students. Then they were given a research seminar in the same topic and an intensive laboratory research experience and the opportunity to observe a demonstration class taught by Dr Ron. We did not know whether these teachers can use our approach effectively, but we did establish that we had found a dramatically effective way of upgrading teachers—possibly far superior to what has been achieved in the usual summer institutes in the United States. I am at present running a similar high school teacher programme supported by the US Office of Education.

Five of the Israeli high school teachers tried our research paper approach in their own schools. The evaluation by the Science Teaching Centre in Jerusalem was that three teachers had produced courses that were good in terms of stimulating

both students and themselves; one teacher was judged to have achieved an excellent result. Consequently this in-service training programme is being repeated and expanded. These are hardly results because of the trivially small numbers, because of the reason set out in the first sentence of this article, and for the usual collection of effects of novelty, teacher enthusiasm and so on. I do not believe that a significant fraction of high school teachers can use our approach. But we have learned that teachers are likely to use research papers in their classes if they feel a comfortable mastery of the papers.

In considering how to ensure a continual input of expertise to teachers, we devised an approach aimed at persuading universities to assume responsibility for the quality of high school teaching. We try to use our most gifted and scholarly professors in introductory university courses to ensure a careful and insightful first contact of students with each subject, so why do we allow undertrained and less competent high school teachers to give the first courses? Unless the teaching of most subjects in high schools is halted, we are led to the need for university involvement in upgrading and maintaining the scholarly competence of high school teachers.

Our approach is to give teachers (eventually also those in social science and the humanities) the previously described in-service research studies course on a narrow aspect of the subject—in our case, molecular genetics. We plan to increase their depth of understanding by having them work with us, essentially as doctoral students, every fifth summer. Then the teachers are expected to attend our weekly departmental colloquium covering broad areas of biology; they will be given an hour's briefing on the background of the day's talk by a member of our faculty. In these ways we hope to upgrade our high school teachers to the point of feeling part of the world of science research so that they know the significant new developments and how they were arrived at. We hope in this way to make the teachers feel competent to introduce students to current scientific activities.

If I have learned anything from my involvement with high schools it is that it is illusory to expect students to learn science other than natural history and some historically well-established facts from teachers who do not know biology to be anything more than its current factual content as explained in the more recent texts. What is missing is the idea of how biology came to be where it is and what is being done to go further. Without such awareness, all biology is a set of happenings and tomorrow's insights degenerate into more unrelated and unsuspected happenings. Biology as an activity, both scientific and cultural, just does not appear. Biology as inquiry can be handled only by inquiring biologists; the philosophy of science can only be discussed by those who know the science. As Oppenheimer remarked, “You can't teach what you don't know”.

The British chemist H. E. Armstrong, working in the 1880s and 1890s at what eventually became City College in London, seems to have been the first person to try using research papers for teaching purposes. It is significant that Armstrong seems to have utilized the same purpose as we have by trying to get his students to put themselves in the positions of people like Priestley and Black in order to work out what to do next and how to do it. This emphasis on the activities of scientists seems to differentiate our work from that of most, if not all, of the other more recent users of research papers. The failure to find the proper classroom emphasis may account for the ending of the other attempts known to me.

Finally, it is worth mentioning that a spin-off from the writing of my book¹ has been the correspondence with readers who have tried related ideas or have worked on the I-lab approach. It has been pleasing to hear from the few others who have tried but, all in all, it has been highly discouraging that there are so few people who have had the courage to try bold new approaches to the LTP.

¹ Epstein, H. T., *A Strategy for Education* (Oxford University Press, London, 1970).

Flandrian Strandline Chronology for the British Isles and Correlation of some European Postglacial Strandlines

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A British postglacial strandline chronology is proposed and correlated with some other parts of Europe. The chronology and correlations are based chiefly on radiocarbon data and drift pumice accumulations.

STRANDLINE correlations, derived from a study of the distribution and origin of drift pumice found on certain European and Arctic postglacial strandlines¹, are presented. The compilations in Tables 1 and 2 derive from critical assessment of carbon-14 datings, strandline chronologies and literature, and drift pumice evidence. Although strandline and radiocarbon data may be unreliable^{2,3}, and relatively few carbon-14 dates are available, the close agreement revealed in Table 2 gives grounds for proposing these correlations, and for suggesting a postglacial strandline chronology for the British Isles.

In common with Andrews³ and Mörner⁴ I believe that an intimate connexion exists between strandlines and climate variations. The culmination of a transgression and of a shoreline construction phase should approximately coincide with the culmination of a climatic optimum. Therefore, strandline surfaces should be essentially synchronous over a wide area, although they may become diachronous towards the centre of previously glaciated areas beyond the reach of transgressions. Strongly developed strandlines (for example, Tapes I of Norway^{5,6}, and the Main Postglacial Shoreline of Scotland⁷) reflect culminations of major shoreline-building transgressions. Most strandlines only mark small climatic and isostatic/eustatic oscillations and are only locally visible. Their existence depends mainly on local variations in isostatic/eustatic interplay, local topography and geology, and destruction or overlap of previously formed strandlines by younger greater transgressions.

A British Strandline Chronology

The data assessed indicate eight strandlines in the British Isles in the period from roughly 7,000 to 2,400 radiocarbon years ago (Table 1). No datings from archaeological sites have been included, because these are not necessarily relatable to the strandline chronology.

The suggested strandlines are designated F 1 to F 8 (F = Flandrian), although early Flandrian strandlines such as the buried ones recognized by Sissons^{7,8} are not included. There

are as many as eight strandlines primarily because, unlike previous chronologies^{7,9,10}, this one covers all the British Isles.

The strandlines were apparently constructed during the following periods: F 1: 7000–6700; F 2: 6450–6200; F 3: 5700–5500; F 4: 5000–4700; F 5: 4100–3900; F 6: 3700–3500; F 7: 3200–3000; F 8: 2500–2400 (all radiocarbon years before present).

Strandline Correlations between Scandinavia, Svalbard and the British Isles

Table 2 shows the correlations suggested throughout the region (Fig. 1). The material comes from many sources, including refs. 4, 5, 7, 9–16 and *Radiocarbon*, 1–12. Many details are treated in ref. 1.

Mörner⁴ correlates his South-West Swedish strandlines

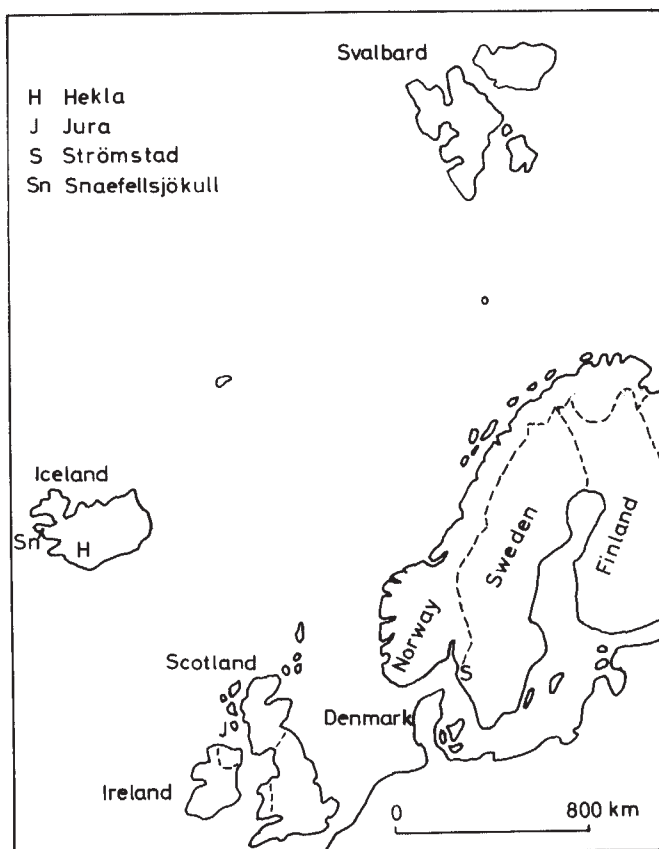


Fig. 1 Region covered by the proposed correlations of postglacial strandlines.

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(Table 2, col. 2) with those of Marthinussen (Table 2, col. 3). Although Mörner's scheme requires some modification (see below), it forms the basis for my correlations. In Table 3 some of Mörner's suggestions are compared with ages proposed by Marthinussen (ref. 5, plate 2), using radiocarbon ages BP.

Marthinussen's suggestion for the age of Tapes I was chiefly based on pollen data from Sweden which are too old to be reliable. Available carbon-14 dates (Table 2, T 182, T 270)

only give an approximate minimum age for the onset of the transgression. Mörner's proposal, based on several radiocarbon datings, is, however, better founded than Marthinussen's. Feyling-Hanssen¹⁷ suggests that Tapes I culminated roughly 6,700 yr ago, and Donner¹⁸ roughly 7,000 yr ago. A strandline (F 1) apparently formed at this time in at least part of the British Isles (Tables 1 and 2, UB 206, Q 638). The ages of Tapes II (PTM-3) and Tapes III (PTM-4) coincide well in the two areas and the latter is clearly identified in the

Table 1 Strandline Data for Eight British Strandlines in the Period 7000 to 2400 BP

Strandline chronology Stephens and Synge	Sissons <i>et al.</i>	Present sug- ges- tion	Carbon-14 date (BP)	Location of sample	Notes on datings	Dating Lab. No.
L 1			8421 ± 157	Airth Colliery, Stirlingshire	Uppermost layer of thin peat bed between late glacial beach and overlying Carse Clay. Pollen	Q 280
			8421 ± 157	Eastfield of Dunbarney (Bridge of Earn), Perthshire	Peat with wood, from peat bed below Carse Clay. Pollen	Q 421
			8354 ± 143	Broombarns, nr. Forgan-denny, Perthshire	Wood from peat below Carse Clay. Pollen	Q 422
			8135 ± 150	Redkirk Point, Dumfries-shire	Wood from stump <i>in situ</i> on peaty bed below Carse-type Clay	Q 637
			8120 ± 135	Ballyhalbert, Co. Down, N. Ireland	Wood from uppermost layers of peat bed under "25-ft" beach. Pollen	Q 214
			7790 ± 160	Ravenglass, Cumberland, England	Wood from buried forest	Y 2427
			7605 ± 180	Carey, Abernethy, Perth-shire	Peat between buried raised beach and overlying Carse Clay. Pollen	NPL 127
			7500 ± 150	Ringneill Quay, Co. Down, N. Ireland	Brackish-water clay deposit immediately preceding building of "25-ft" beach	Q 632
			7345 ± 150	Sandyknowe Bridge, Lochar Water, Dumfriesshire	Wood fragments from just above base of fine silty sand (Carse) overlying fluvio-glacial material	GU 65
			7426 ± 136	Newbie Cottages, Solway Firth, Dumfriesshire	Top of peat bed overlain by Carse deposits, underlain by fluvio-glacial material	GU 64
L 1/2			7254 ± 101	Woodgrange, Co. Down, N. Ireland	Top of layer of organic detritus underlying marine sand, transgression contact (see I 1199, LJ 903)	I 1198
			6955 ± 100	Drumskellan, Co. Donegal, Eire	Wood, embedded in raised beach—therefore max. age of beach	UB 206
			6645 ± 120	Lochar Moss, Dumfriesshire	Peat from bed overlying the Carse Clays	Q 638
			6550 ± 300	Woodgrange, Co. Down, N. Ireland	Organic content in clay, from transgression contact (see I 1198, I 1199)	LJ 903
			6244 ± 140	Gatehouse of Fleet, Kirkcud-brightshire	Wood from top of peat lens near the top of a thick beach deposit	Q 818
			6159 ± 120	Newton Stewart, Wigtown-shire	Wood in sediments probably belonging to "25-ft" beach	Q 639
			5734 ± 129	Silverdale Moss, N. Lancs., England	Oxidized fen peat immediately below marine clay. Pollen	Q 256
			5700 ± 170	Benbecula, Outer Hebrides, Scotland	Wood from beach, ca. 0.5 m under O.D.	I 1543
			5492 ± 130	Flander's Moss, Stirlingshire	Wood peat, 10–12 cm above upper surface of Carse Clay	Q 533
			4740 ± 110	Cushendun, Co. Antrim, N. Ireland	Wood overlying grey silt marking late stage of marine transgression, overlain by 1 m coarse gravel. Pollen	Q 373
L 3			4100	Exact age and site not known	Peat in Forth valley, just below P.G.3 (Sissons ⁷)	?
			3730 ± 130	Sutton, Co. Dublin, Eire	Estuarine peat, under marine gravels deposited during a regression	D 31
			3687 ± 110 (av. of 2)	Moreton, Cheshire, England	Wood from tree lying in peat; roots extend into marine silty clay over 1 m thick	Q 620
			3656 ± 150	Heathershot, Bridge of Allan, Perthshire	Wood and hazel nutshells just below "Carse Clay" and above gravel and clay	Q 666
			3572 ± 64	Linwood Moss, Renfrew-shire	Wood fragments from base of peat grading down into grey silt overlying Late-glacial clay	Birm 2
			3513 ± 56	Linwood Moss, Renfrew-shire	Peat from basal part of peat (see Birm 2)	Birm 13
			3249 ± 160	Littleward, Kippen, Stirling-shire	Wood from immediately below assumed "Carse Clays" (as Q 666)	Q 667
			3125 ± 150	Woodgrange, Co. Down, N. Ireland	Bottom of layer of organic detritus above marine sands, regression contact (see I 1198, LJ 903)	I 1199
L 4 L 4/5	P.G.4	F 8				

For explanation of L.1, L 1/2 see notes to Table 2.

Table 2 Suggested Strandline Correlations

North Norway (mainly after Marthinussen ⁵)		South-West Sweden (after Mörner ⁴)	Mörner's correlation of Marthinussen	Scotland-Ireland- North-West England ^a	British Isles ^b	Suggested correlations North Norway ⁵		Svalbard
(T 182)	7750 ± 150 (? Onset of transgression)	7750 (Onset of transgression)		(Q 280) 8421 ± 157 (Q 637) 8135 ± 150 (Q 214) 8120 ± 135 (Y 2427) 7790 ± 160 (NPL 127) 7605 ± 180	L 1			7720 ± 110 (U 130) 17.0 m
(T 270)	7400 ± 150 (pre-Tapes I)	Transgression		(Q 632) { 7500 ± 150 7345 ± 150 (GU 65) 7426 ± 136 (GU 64) 7254 ± 101 (I 1198) 7220 ± 175				
		7050-6900 PTM-2 (Transgressive)	Tapes I	(UB206) 6955 ± 100	L 1/2	F 1	Tapes I P	
		Regression						
		Transgression		(Q 638) 6645 ± 120 (LJ 903) 6550 ± 300				Tapes I/II { 7035 ± 110 (U 112) ^c 6.2 m U.P. 6915 ± 110 (U 33) ^c 9.8 m U.P. 6875 ± 110 (U 111) ^c 8 m U.P. 6785 ± 110 (U 116) ^c 9.0 m U.P. 6700 ± 70 (U 618) 9.8 m U.P. 6625 ± 110 (U 36) ^c 8.8 m U.P. 6526 ± 80 (Birm 37) 18.5 m 6485 ± 100 (St 2776) regression
(T 185)	6350 ± 150 (on Tapes IV)	6450-6200 PTM-3 (Transgressive in late stage)	Tapes II	(Q 818) 6244 ± 140		F 2	Tapes II P	
(T 267)	6250 ± 200 (on Tapes II)			(Q 639) 6159 ± 120				6335 ± 100 (U 107) ^c 7.6 m U.P. 6240 ± 80 (St 2018) 30.5 m
(U 79)	6245 ± 110 ^c (on Tapes)	Regression						
(T 296)	6100 ± 150 { post-Tapes II pre-Tapes III }							
		5900-5550 PTM-4A (Trans- PTM-4B gressive)	Tapes III	(Q 256) 5734 ± 129 (I 1543) 5700 ± 170				
(U 160)	5745 ± 150 ^c (pre-Tapes IV) ^d							
(T 184)	5700 ± 150 (on Tapes III)							
(T 183)	5500 ± 150 (on Tapes III)			(Q 533) 5492 ± 130	L 3 P.G.1	F 3	Tapes III P	Tapes III 5550 ± 140 (St 2665) transgression
		Regression 5050-4900 (Transgressive)	Tapes IV		L 2			
(T 126)	4820 ± 160 (on Tapes IV)			(Q 373) 4740 ± 110		F 4	Tapes IV P	Tapes IV 5070 ± 100 (Mo 416) 50 m
		Regression			P.G.2			
		4700-4600 PTM-5B (Transgressive)						
(T 266)	4500 ± 150 (on Tapes IV)		N ₅					4745 ± 120 (St 2666) regression
		Regression						4500 ± 90 (U 203) 9.7 m
(T 505)	4130 ± 100 (near N ₄)							
(T 186)	4100 ± 100 (on N ₄)	4250-3950 PTM-6 (Transgressive)		? 4100 P	P.G.3	F 5	N ₄ P	N ₄
(T 244)	4100 ± 150 (on N ₄)							
		Regression		(D 31) 3730 ± 130 (Q 620) 3687 ± 110 (av. of 2)	L 3			4155 ± 90 (U 34) ^c 2 m ca. L.P. 4070 ± 100 (U 126) ^c 5.8 m 4060 ± 100 (Mo 418) 20 m 4010 ± 80 (St 1959) 14.8 m 3825 ± 100 ^c (St 2219) 14.8 m

(U 99)	3575 ± 90 ^c (post-Tapes IV) ^d	3600–3250 (Transgressive)	PTM–7	(Q 666) (Birm 2) (Birm 13)	3656 ± 150 3572 ± 64 3513 ± 56	F 6			
(T 353)	3165 ± 100 ^e	Regression		(I 1199)	3125 ± 150	F 7	N ₃	N ₃	3190 ± 130 (Mo 420) 11 m
(T 304)	3130 ± 110 (post-N ₄ , pre-N ₂)		PTM–8						
(T 351)	3070 ± 100 (post-N ₄ , pre-N ₂)	(Transgressive)							
(St 926)	2780 ± 65 (post-N ₄ , pre-N ₂)	Regression							
(T 385)	2710 ± 90 (post-N ₄ , pre-N ₂)		PTM–9A	N ₂		F 8	N ₂	N ₂	2400 ± 120 (Mo 419) 5.5 m
(T 243)	2450 ± 100 (on N ₂)	(Transgressive)				L 4 L 4/5			
		Regression	PTM–9B						
(T 350)	2200 ± 100 (post-N ₂)	(Transgressive)		N ₁		P.G.4			1550 ± 120 (Mo 421) 5 m

a—See Table 1 for details of locality, material and horizon.

b—L 1, L 2, etc., after Stephens¹⁰; L 1/2, L 3, etc., after Syngé and Stephens⁹; P.G.1, etc., after Sissons⁷; F 1, etc., see Table 1.

c—135 years added to date in *Radiocarbon* to convert to NBS standard³².

d—The youngest Tapes strandline stated to be between these³³.

e—305 years subtracted from date in *Radiocarbon* to allow for age of seawater affecting shell samples (ref. 4, pp. 15–16).

f—400 years subtracted from original dating result by Hoppe *et al.*¹¹—“seawater” age correction.

P—Main drift pumice accumulations on these strandlines in Norway and British Isles.

U.P.—Upper drift pumice accumulation level.

L.P.—Lower drift pumice accumulation level.

British Isles where Sissons⁷ calls it the Main Postglacial Shoreline and I have called it F 3. Evidence also exists (Table 1, Q 818) for a strandline (F 2) in the British Isles, equivalent to Tapes II. Tapes IV is given a greater age by Möner than by Marthinussen, and corresponding shorelines in the British Isles (F 4) and Svalbard are also given slightly lower ages than Möner suggests (Tables 1 and 2, Q 373, St 2666). Marthinussen's 4500 date seems too young, and may refer to his N₅ strandline. In Norway pumice accumulations occur on all these Tapes strandlines (see refs. 19, 20), but the three lowest ones are probably produced by secondary drifts of material washed off peripheral, re-submerged, stretches of Tapes I (ref. 1).

A regression (Table 2, St 2776) roughly 6,450 yr ago is identified¹² in North-Eastern Svalbard. This may correspond to the interval between Tapes I and II, or mark a somewhat early regression from Tapes II, or mark an oscillation corresponding to one recorded by Möner⁴ in parts of southern Sweden. Another transgression occurred later (Table 2, St 2665), and apparently reached roughly the same height as the earlier one (Blake^{14,15}, see dates in Table 2). Final regression from this level occurred about 4,750 yr ago¹² (Table 2, St 2666). Hence this composite strandline not only corresponds well with Tapes I–IV of North Norway and the equivalent level in South Sweden (and Denmark) as Blake¹⁴ says, but also with equivalent strandlines in the British Isles. The upper pumice level in North-East Svalbard is on this Tapes I–IV shoreline complex, and the pumice (also that which Blake¹⁴ found at this level in Canada) may have been washed ashore at any time prior to the final regression.

In the British Isles the oldest established pumice occurrences found (with the possible exception of one on Jura (Fig. 1), (J. Mercer, personal communication)) have been made on the F 3 strandline corresponding to Tapes III (or perhaps a composite Tapes I–III or II–III level), and in Mesolithic sites dating from within the full period covered by F 1–F 4 (ref. 1). This pumice is the same type as that found on equivalent Norwegian strandlines.

Mörner⁴ correlates Marthinussen's N₅ line with his PTM–5B and PTM–6, allotting N₄ to PTM–7, a line which he dates 500–650 years younger than Marthinussen's N₄. He states that N₅ is a double line and that because the N₅ and N₄ lines are very close at the localities which provided the dated samples (Table 2, T 186, T 244) his interpretation can be justified. Apart from Marthinussen's^{5,19} references, however, to a possible extra line between N₅ and N₄ there is no mention in the literature of N₅ being a double line. Hansen¹⁶ identifies no line at that level in the area of North Norway he studied, but he found N₄ to be distinct, especially in the inner part, and gives a carbon-14 dating of it from the outer part of his area (Table 2, T 505). Marthinussen's N₄ line is distinct, well determined and well dated in Norway (Table 2, col. 1) and contains the lowest important pumice level there. A strandline of the same age (Table 2) also contains the lowest recorded pumice accumulation in Svalbard and the British Isles, though scarcely any British or Svalbard strandline pumice is black, a contrast to the large amount in the Norwegian N₄ level. This difference is not important, however, because a dominant wind could have blown ashore on the Norwegian coast nearly all of a black pumice raft from a contemporary eruption.

At Strömstad, in the extreme west of Sweden, the lower pumice level—assuming the single specimen recorded²¹ really belongs to an accumulation—corresponds to either Möner's (ref. 4 plate 6) PTM–6 or his PTM–5B lines (respectively about 20 m and 25 m above sea-level at Strömstad). PTM–7, which Möner correlates with N₄, should on the same criterion be about 12 m a.s.l. at Strömstad, which is nearly half the height of the pumice find. The interpretation given by Möner⁴ of dates published by Berglund²², and supposedly referable to Möner's PTM–5B and PTM–6 strandlines, suggests ages of about 4,550 yr for the former and about 4,100 yr for the latter. The succeeding regression and the PTM–7 strandline are chiefly

dated on pollen analytical and faunal evidence. The latter, according to Möner, indicates an age for PTM-7 of 3,600–3,250 yr, but another interpretation is possible. The warmth-loving faunal association he cites appeared as early as 4,200–4,500 yr ago. Furthermore, he attributes the transgression leading to PTM-6 a greater eustatic rise in sea-level than the one leading to PTM-7, which should imply that PTM-6 was constructed during a greater climatic optimum than PTM-7 (ref. 4, pages 422–5). This transgression and optimum correspond exactly with Fairbridge's²³ Younger Peron Submergence. Pollen evidence indicates a distinct positive climatic oscillation at a time equivalent to the construction of N₄ (around 4,100–4,000 yr ago) (B. and K.-D. Vorren, personal communication). Wiseman²⁴ and Lamb *et al.*²⁵ give sedimentological and climatic data, respectively, supporting this. The strong development of N₄ compared with other post-Tapes strandlines also suggests its construction during an important climatic optimum.

Table 3 Summary of Chronology Data presented in Text

Chronologies of Möner	Marthinussen (and Svalbard—S)	British chronology proposed here	Suggested age (BP) for culmination of strandline construction	Pumice accumulations (probably only first and last ones are primary drifts)
PTM-2	Tapes I	S	F 1	7000–6700 N., ? B.I., Sw.
PTM-3	Tapes II	S	F 2	6450–6200 N., ? B.I.
PTM-4	Tapes III	S	F 3	5700–5500 N., B.I.
PTM-5A	Tapes IV	S	F 4	5000–4700 N., S.
PTM-5B	N ₅			4400–4300 N. (minor)
PTM-6	N ₄	S	F 5	4100–3900 N., B.I., S., ? Sw.
PTM-7		S	F 6	3700–3500
PTM-8	N ₃	S	F 7	3200–3000
PTM-9A	N ₂	S	F 8	2500–2400

Hence, I believe Marthinussen is correct in placing N₄ in the period 4,100–3,900 yr ago and Möner is wrong in correlating it with his PTM-7 line. It must instead be correlated with PTM-6, even if that line is less distinctly developed in South-West Sweden. N₅ may correlate with PTM-5B.

Probably no established Norwegian strandline can be correlated with Möner's PTM-7 line. Marthinussen^{5,19,20} describes three strandlines N₃, N₂ and N₁, younger than about 4,000 yr. He dates N₂ to about 2,450 years ago (Table 2, T 243), and in the same paper⁵ publishes, without comment, a newly obtained dating of 3070 ± 100 (Table 2, T 351). This, and two other dates (Table 2, T 353, T 504) obtained by Marthinussen²⁰ and Hansen¹⁶ respectively, may refer to the N₃ line, as Marthinussen himself (ref. 5, plate 2) seems to imply. A strandline (F 7) has probably formed at this time in at least part of the British Isles (Tables 1 and 2, I 1199) and also in Svalbard (Table 2, Mo 420). This strandline, apparently recognizable in Norway, Ireland and Svalbard, formed in the period 3,200–3,000 yr ago and consequently cannot equate with Möner's PTM-7 line, but probably correlates with PTM-8 (Table 2). This age coincides with an amelioration recognized in the palynological record of South-West Scotland²⁷ as well as many other parts of Europe²⁸. It followed a marked cold spell about 3,550–3,350 yr ago^{29–31}, which corresponds in time with the second half of the period of formation Möner attributed to his PTM-7 line and makes this difficult to accept (B. and K.-D. Vorren, personal communication). An age of about 3,700–3,500 yr for this line is more reasonable and its elevation would have been brought about by the above-mentioned cold spell, thus putting Möner's PR-8 regression slightly back in time. This strandline will furthermore correlate with F 6 in the British Isles, the existence

and age of which seem well established (Table 1, Q 620, Birm 2, Birm 13). If N₃ is to be allotted an age of 3200–3000 years, no strandline equivalent to PTM-7 and F 6 has been distinguished in Norway. No equivalent dates exist for a strandline on Svalbard.

These suggestions for the ages of N₅, N₄ and N₃, and of equivalent strandlines elsewhere, correspond well with data given by Wiseman²⁴, Fairbridge³⁰, and Frenzel³¹, although Frenzel's data disagree with Wiseman's and my suggestions concerning the climate about 4000 BP.

Finally, a strandline dating from the onset of the marked climatic deterioration about 2,500 yr ago is clearly recognizable in all the countries considered here (Table 2).

The chief results of the above discussion are summarized in Table 3.

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ADDENDUM. A paper by Berglund³⁴ arrived too late to be incorporated in Table 2 and the text. His data generally support the above correlations, especially as regards N₄ and PTM-6. But a strandline equivalent to Tapes IV is attributed an age 300–600 yr greater than that given here. Hence, the age of this important strandline seems unusually variable from area to area.

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Oogenetic Origin of Messenger RNA for Embryonic Synthesis of Microtubule Proteins

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Microtubule protein in RNA is present in considerable quantities in the unfertilized egg. After fertilization, the synthesis of microtubule proteins begins and proceeds at an increasing rate during cleavage.

THE protein synthetic programme of early embryonic development seems to involve not only concurrently-transcribed RNA templates, but also messenger RNA (mRNA) synthesized during oogenesis and stored in the egg cytoplasm¹⁻⁴. So far as mRNA produced on embryonic genomes is concerned, we have a specific example in the complex of polynucleotides, sedimenting at about 9S, on which are encoded histones of embryonic chromatin. A large part of the histone synthesis depends on continuous entry of this mRNA into the polyribosomes^{5,6}. It is a matter of interest and importance to identify, similarly, a specific protein or group of proteins synthesized on preformed (sometimes called "maternal") mRNA already present in the unfertilized egg.

We found in earlier work that a dose of actinomycin D sufficient to suppress almost completely the synthesis of high molecular weight RNA in sea urchin embryos had little or no effect on the incorporation of ³H-leucine into the monomeric proteins of cytoplasmic microtubules, even over extended periods. The insensitivity of microtubule protein labelling to transcription block, contrasting strongly with the synthesis of histones and other chromosomal proteins, led us to suggest that microtubule proteins might offer a specific example of those encoded on maternal mRNA⁷.

The proof of such a proposal requires attention to alternative explanations that do not apply to the maternal mRNA situation as a whole, for while the latter can be established in a straightforward way from the actinomycin results, and is in any case a unique interpretation of results that do not involve inhibitory drugs^{4,8,9}, the labelling of a single species or group of proteins during transcription block might be explained differently. If, on the other hand, the alternatives can be ruled out, the maternal mRNA theory, with its important consequences for regulation of development, is further strengthened.

Among the alternatives considered, those that appeared most serious were the following. (1) "Chemical enucleation" with actinomycin might not be completely effective, that is, mRNA for microtubule proteins might be part of a special class of RNA molecules the transcription of which in the nucleus is exceptionally resistant to the drug. Such a class would be so small as to escape detection in ordinary labelling experiments, so that RNA labelling data would be inadequate by themselves to exclude the possibility. (2) Synthesis of RNA takes place on cytoplasmic as well as nuclear genomes in early sea urchin development. While the cytoplasmic transcription, which is chiefly mitochondrial¹⁰⁻¹³, can be inhibited with actinomycin, even large doses do not suppress it entirely¹³. Messengers for microtubule protein synthesis might thus be among the products of cytoplasmic transcription. (3) The presence of a pool of microtubule proteins in the egg and at all later stages⁷

suggests the possibility of post-transcriptional modification, with enzymatically-catalysed addition of labelled amino-acids or their metabolites not involving ribosomal peptide bond formation¹⁴. If this were the case, the observed labelling of microtubule proteins might have nothing to do with mRNA.

The results now to be described yield the following results on these points. (1) The presence of a nucleus is not required for microtubule protein synthesis; (2) RNA synthesized in the cytoplasm does not provide the templates for microtubule proteins; (3) labelling of these proteins with exogenously supplied tracer amino-acids does take place through translation of mRNA in a normal ribosome-dependent system. We can therefore confirm the hypothesis that templates for synthesis of microtubule proteins in the embryo are already present in the cytoplasm of the unfertilized egg.

Synthesis in Enucleate Fragments

Cultures (10 ml.) of nucleate and enucleate sea urchin egg halves, prepared by centrifugal cleavage^{15,16}, were activated parthenogenetically and incubated in sterile seawater containing 5 μ Ci/ml. of ³H-leucine for 2 h. At the end of the incubation, 1 ml. of packed whole eggs, resuspended in 10 ml. of sterile seawater with 10⁻³ M emetine (which stops protein synthesis¹⁷), was added to the half-egg cultures as carrier. Purification of microtubule proteins and estimation of their incorporated radioactivity were as described in the legend to Fig. 3 and in more detail in our earlier report⁷.

The activated egg fragments were found to incorporate tracer amino-acid into microtubule proteins whether or not a nucleus was present. Since leucine pool sizes and permeabilities are not known for half-eggs, and since they are probably different from those of normal zygotes (owing to the centrifugal redistribution of all cytoplasmic solids), estimates of the absolute rates of microtubule protein synthesis cannot be made. A comparison between nucleate and enucleate halves can be made, however, using the ratios of incorporated microtubule protein radioactivity to total protein radioactivity. As Table 1 shows, such ratios do not differ very greatly as between nucleate and enucleate half-eggs. Small differences do not, of course, affect the argument. In view of the extremely low cross-contamination of enucleate fragments with the more slowly sedimenting nucleated ones¹⁵, it is clear that physical enucleation, like chemical inactivation of gene transcription, does not prevent the labelling of microtubule proteins. Thus there is no class of RNA molecules transcribed in the nucleus after fertilization that is required.

Translation

There is a reproducible difference between the intracellular distribution of high molecular weight RNA¹³ labelled in parthenogenetic enucleate half-eggs and that produced in half-eggs that have been fertilized (Fig. 1). The fertilized fragments, which contain a functional nucleus (and develop to larvae), make some RNA that associates very quickly with polyribosomes, as is the case in normal development^{17,18}. When the polyribosomes from fertilized half-eggs are dissociated by the action of EDTA, sedimentation velocity of the labelled RNA is reduced in the same way as is observed for functional mRNA in embryos (Fig. 2 and ref. 18). By contrast, the enucleate half-eggs, which load ribosomes onto mRNA and label nascent chains in a way that is for some time indistinguishable from

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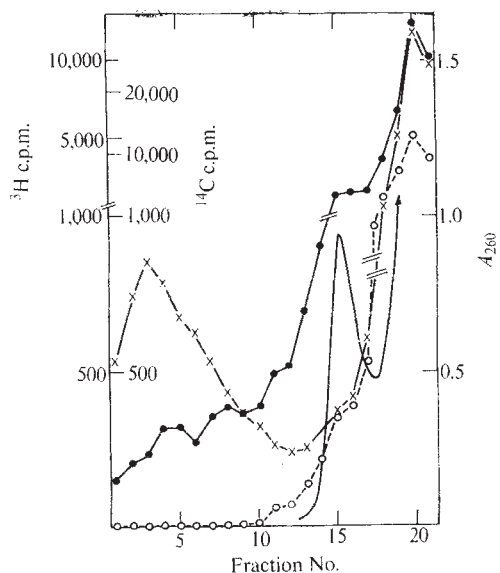


Fig. 1 Newly-synthesized RNA and proteins in enucleate half-egg polyribosomes. Half-eggs were prepared by centrifugation in sucrose-seawater gradients as described¹⁵. Enucleate half-eggs were divided into two cultures. Those in the first culture were activated using hypertonic seawater¹⁶, and those in the second culture were inseminated. Following activation, an additional 50 U ml.⁻¹ of penicillin-streptomycin was added to each culture. Flasks were wrapped in aluminium foil to exclude light and thus to prevent growth of algae. Both mixtures were made 100 μ Ci ml.⁻¹ in ³H-5-uridine and incubated for 2 h. Ten minutes before the end of incubation, 1 μ Ci ml.⁻¹ ¹⁴C-leucine was added to each culture. Polysomes and sucrose gradient analysis were done as described earlier¹⁸, except that the gradients were centrifuged for 4 h. ●—●, ³H-Uridine incorporation into fertilized half-eggs; ○—○, ³H-uridine incorporation into activated half-eggs; ×—×, ¹⁴C-leucine incorporation into activated half-eggs. ¹⁴C-Leucine incorporation into fertilized halves is not shown, but displayed a similar pattern with somewhat more label incorporated. —, A_{260} in the monosome region.

the normal, make no RNA that associates detectably with polyribosomes (Fig. 1). This differential behaviour is highly reproducible¹⁹. Hence RNA made in the cytoplasm following fertilization cannot contain messengers encoding microtubule proteins, nor indeed any other mRNA translated on ordinary polyribosomes. It might be that microtubule proteins are made on a special class of polyribosomes, not so far described, that is not isolated by the ordinary means. This is rendered very unlikely by results to be discussed later.

Activation of Protein Synthesis

Actinomycin and ethidium bromide can be used together in conditions that block nuclear and cytoplasmic RNA labelling¹⁹⁻²¹. When this is done, the normal pattern of

Table 1 Microtubule Protein Synthesis by Artificially Activated Nucleate and Enucleate Half-eggs of *Arbacia*

Culture	Total incorporation (c.p.m.)	Specific activity of MT* protein peaks	SA MT proteins† Total incorporation
Nucleate	132,850	10,800	0.081
Enucleate	221,800	11,000	0.050

* Counts recovered in microtubule protein peaks on acrylamide gels divided by weight of chart paper under A_{600} peak of microtubule proteins. Equal amounts of carrier eggs were added to each culture before homogenization (in the presence of 10^{-3} M emetine). The contribution of carrier microtubule protein far exceeds endogenous microtubule protein, so that differences in sizes of microtubule pools between nucleate and enucleate halves become negligible, and the A_{600} peak becomes a recovery marker, eliminating correction for losses of microtubule protein during processing.

† Division of specific activity of microtubule proteins by total incorporation eliminates complications arising from differences in amino-acid pool sizes, rates of uptake, mass of cells, and extent of parthenogenetic activation.

increase in amino acid incorporation is observed at least through the first cleavage cycle (Table 2). Thereafter, viability of the drug-treated embryos declines, possibly because of damage to the mitochondria (A. L. Hunter and P. R. G., unpublished data), and the experiments have to be terminated. The critical point is that suppression with drugs of both nuclear and cytoplasmic RNA synthesis fails to alter the characteristic activation of protein synthesis, with its massive recruitment of ribosomes onto mRNA (for example, ref. 22), that follows fertilization or artificial parthenogenesis. Exposure of eggs to ethidium bromide plus actinomycin for 1 h before fertilization and for 75 min longer thereafter had, furthermore, no detectable differential effect on microtubule protein synthesis relative to the bulk incorporation (data not shown here). These results contribute to the conclusion that RNA transcribed in the cytoplasm does not contain messages for the synthesis of microtubule proteins.

An independent supporting observation is that of Craig and Piatigorsky²¹, who found no differences between gel electropherograms of proteins synthesized in ethidium-treated half-eggs and untreated ones.

Inhibition by Emetine

Emetine is a highly efficient and specific inhibitor of polypeptide chain elongation on polyribosomes of sea urchin embryos¹⁷. At a dose of 10^{-3} M in the systems here described, it inhibits incorporation of ³H-leucine into total proteins by more than 97%. Simultaneously, it abolishes all detectable incorporation of label into microtubule proteins. That labelling must therefore take place by way of ribosome-mediated polypeptide chain assembly, rather than by post-transcriptional modification of pre-existing chains.

Labelling of Microtubule Proteins

A very small incorporation of radioactive amino-acids into microtubule proteins occurs in suspensions of unfertilized eggs (Fig. 4). Some part of this might be due to an unavoidable small (about 1%) contamination by oocytes and spontaneously activated eggs, but the reproducible appearance of radioactivity co-migrating with microtubule proteins from cultures of unfertilized eggs suggests that the synthesis may in fact occur as part of the maintenance metabolism of the ootid.

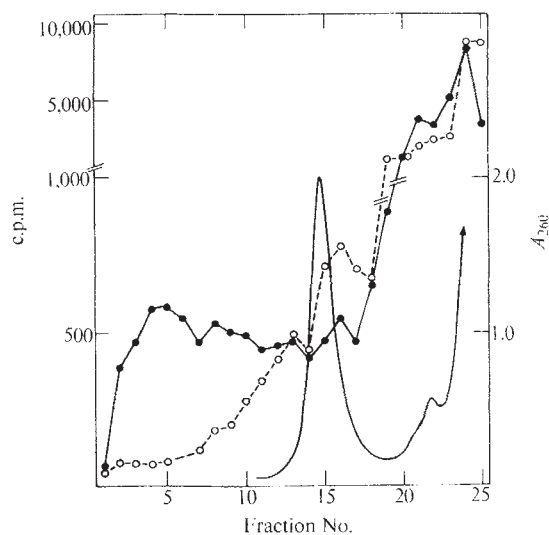


Fig. 2 EDTA-sensitivity of polyribosomal radioactive RNA. Enucleate half-eggs were treated as described in Fig. 1, except all were fertilized and no ¹⁴C-leucine was added. Polysomes were prepared as described elsewhere¹⁷. The 10,000g supernatant was divided into two portions, one of which was made 40 mM in EDTA. Both were layered on 11 ml. 7-47% sucrose gradients and centrifuged at 40,000 r.p.m. for 90 min at 4°C in an SW 41 K Beckman rotor. ●—●, Control; ○—○, EDTA treated; —, A_{260} of control gradient. Gradient of EDTA-treated polysomes had A_{260} peak in fraction 18.

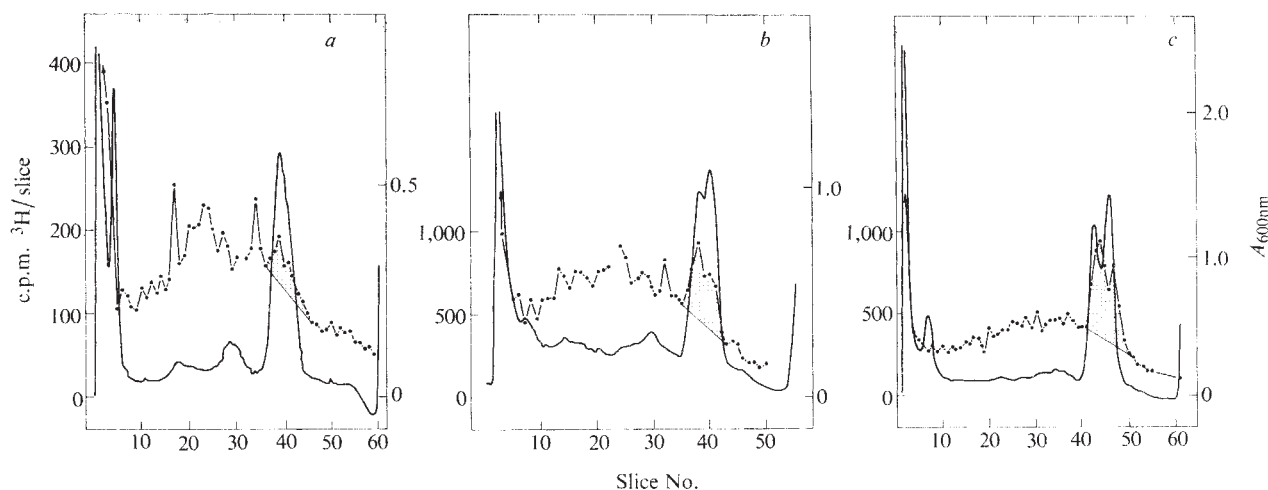


Fig. 3 Polyacrylamide gel electrophoretic analysis of microtubule protein synthesis by embryos cultured in actinomycin D. Eggs of *Arbacia punctulata* were incubated at 20°C for 90 min in sterile seawater (plus penicillin-streptomycin) containing 20 µg ml.⁻¹ actinomycin D in a foil-wrapped flask. At the end of that time the eggs were fertilized in the actinomycin which was present continuously throughout the experiment. Subcultures of embryos were incubated for 30 min with 1 µCi ml.⁻¹ ³H-leucine at various stages; they were then made 10⁻³ M in emetine and aliquots removed for determinations of protein³² and total incorporation. The remainder of the cultures were used for the preparation of microtubule proteins by vinblastine sulphate precipitation for gel electrophoresis (detailed methods given in refs. 7 and 33). The specific activities of soluble proteins were determined from the 150,000g supernatants from which microtubule proteins were to be prepared. Labelling was done at three stages in this experiment: *a*, immediately after fertilization; *b*, at the eight cell stage; *c*, at the sixteen cell stage. Gels were stained with fast green, and after destaining scanned at 600 nm with a Gilford model 240 spectrophotometer. Gels were then sliced into 1-mm thick slices which were prepared for scintillation counting^{7,33}. Electrophoresis direction is from left to right. The solid trace (—) represents the *A*₆₀₀ of the gels while the counts per slice are represented by connected dots (●—●). The stippled regions indicate the areas used for summing the total c.p.m. incorporated into microtubule proteins. Specific activity (SA) was calculated by dividing the total c.p.m. in a stippled area by amount of microtubule proteins present in the *A*₆₀₀ peak (determined by weighing the area under the *A*₆₀₀ trace). The gels displayed here are representative of those used to obtain the data of Figs. 4 and 5.

More important perhaps is the fact that microtubule proteins are synthesized at all times after fertilization, including the first cleavage cycle (Fig. 4). This resolves at least qualitatively earlier arguments about whether or not characteristic structural proteins of the mitotic apparatus are synthesized during cleavage divisions.

Even the unfertilized egg seems to synthesize some microtubule protein, and so we must consider the possibility that the mRNA is synthesized concurrently at that time, and although its synthesis ceases or becomes redundant after fertilization, the residual mRNA is stable enough to allow continued translation for many hours during development. This would not alter what is now the fact that microtubule mRNA is present in the egg, but it would mean that this particular message is a relic of the ootid's maintenance transcription, rather than an mRNA stored during oogenesis for later translation.

There are several grounds on which this possibility can be excluded or at least rendered unlikely. First, it must be recalled that the sea urchin egg is an ootid whose maturation divisions, with their associated biosynthetic cycles, have been completed. In the normal case, the spawned eggs have been

ootids for a matter of weeks to months, depending on species and the time of year. Spawned ootids are ready for fertilization and normal development from the first instant of spawning^{16,22} so that there is no obligatory interval of transcription preceding fertilization, however brief. The ootids seem, furthermore, to synthesize no RNA at all, neither in the ovary nor after spawning⁸. Thus, while failure to label does not prove absence of synthesis, the biology of sea urchin eggs together with that failure argues against an ongoing production of mRNA up to the moment of fertilization.

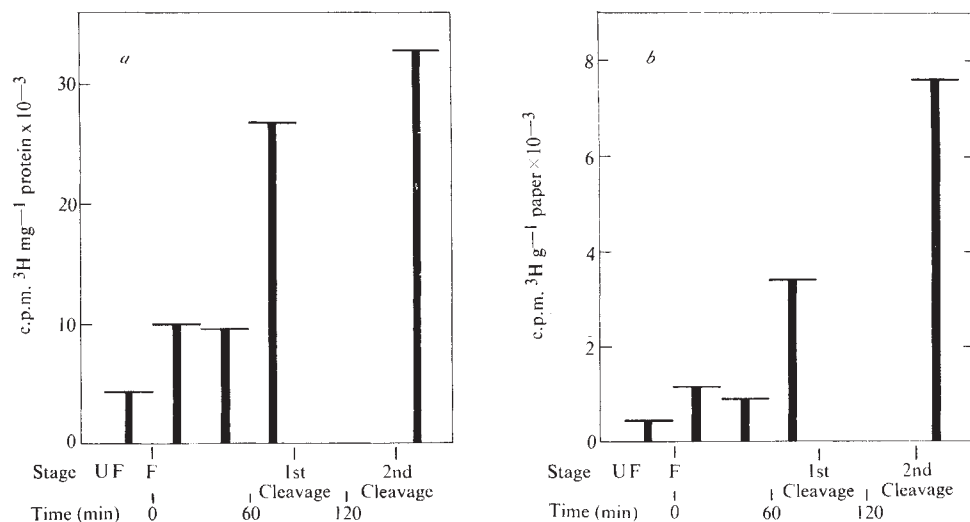
More cogent, perhaps, is the pattern of increased incorporation into total and microtubule proteins after fertilization. This was examined in eggs and embryos labelled with ³H-leucine in the presence and absence of actinomycin D, followed by purification and analysis of the labelled proteins. Specific activities of microtubule proteins labelled at various intervals were compared with the specific activities of total or soluble proteins labelled concurrently. (Use of the soluble protein specific activities eliminates the hazard of variable homogenization efficiency at different stages.) It should be noted that the total protein content per embryo is invariant²³ and that the pool of soluble microtubule proteins does not change significantly in size⁷. In the critical period from fertilization to first cleavage, *Strongylocentrotus purpuratus* embryos increase their rate of incorporation into microtubule proteins by increments that are, conservatively, as large as those for the total (Fig. 4). There is in fact a trend of microtubule protein synthesis to increase faster than total synthesis, but that is best demonstrated over longer developmental intervals (R. A. R., unpublished data). The situation in *Arbacia punctulata* is the same, although in this species there is rather more background radioactivity on the gels (Fig. 3), making specific activity estimates less certain than in *Strongylocentrotus*. There is no doubt, nevertheless, that incorporation into microtubule proteins increases at least as fast as it does for all other proteins following fertilization. In fact, when actinomycin is present, it increases much faster (Fig. 5). This is a particularly clear situation, in which there can be no significant contribution of newly-synthesized microtubule mRNA, and in which there cannot yet have been a significant decay of the bulk maternal mRNA²⁴⁻²⁶.

Table 2 Effect of Actinomycin plus Ethidium Bromide on the Post-fertilization Rise in Protein Synthesis in Embryos of *Arbacia punctulata*

Time of labelling (min)	Control (Incorporation, c.p.m./95,000 embryos)	Drug treated
Unfertilized (15 min)	270	170
0-15	1,270	1,450
15-30	1,430	2,245
30-45	5,500	3,350
45-60	3,500	2,550
60-75	3,170 (first cleavage)	2,270
75-90	4,130	2,630 (first cleavage)

A culture of washed eggs was divided in two. One was made to 20 µg ml.⁻¹ in actinomycin D and 10 µg ml.⁻¹ in ethidium bromide. Both cultures were incubated in the dark for 1 h. A pair of aliquots was removed from each for a 15-min incubation with 0.5 µCi ml.⁻¹ ³H-leucine. The eggs (or embryos in subsequent incubations) were lysed with 0.5% SDS, precipitated with 7% TCA and washed on to 'Millipore' filters for counting. Both cultures were then fertilized, and a series of 15-min pulse-labellings with ³H-leucine was performed.

Fig. 4 Specific activities of total and microtubule proteins of *Strongylocentrotus purpuratus* eggs and early stage embryos. Eggs and embryos were incubated for 30 min in the presence of $1 \mu\text{Ci ml}^{-1}$ ^3H -leucine. Preparation and specific activity determinations of total proteins (a) and microtubule proteins (b) were described in the legend to Fig. 3. Pulse intervals are indicated by the crosspieces on top of the bars. UF, Unfertilized; F, fertilized.



It must be understood that the rising incorporation means a rapidly rising absolute rate of synthesis for total proteins. This has been demonstrated by several independent means^{22,27-29}. The absolute rate of synthesis increases very rapidly during the first cleavage cycle to a value at least ten, and possibly as much as seventy, times that of the unfertilized egg. This is accompanied by a change in the polyribosome content from an amount too small to be detected by absorbance to approximately 30% of all the ribosomes in the egg²⁶.

Hence microtubule proteins are synthesized at a rapidly rising rate after fertilization, as are many other proteins. This takes place in the absence of any new mRNA, so that microtubule mRNA already present in the ootid must support the increase. This could happen, in principle, if existing and functioning microtubule mRNA were simply translated at a rate ten to seventy times greater, but there is no basis on which to assume that translation velocities can vary from one eukaryotic mRNA to another in the same system (for example, ref. 30). For total protein synthesis in embryos it is unlikely that translational velocity changes significantly at fertilization²⁷ or at any other time³¹. The rates of chain elongation being therefore almost certainly constant, an increasing rate of synthesis coupled with a large increase in the number of

polyribosomes means that mRNA is being recruited into the translational apparatus. This is, of course, the "masked" mRNA principle²⁴, the validity of which seems no longer to be in doubt²⁶.

Thus there is a store of microtubule mRNA, only a fraction of which is in use before fertilization—a store from which recruitment permits the development of a pattern of increasing synthesis with time. That this mRNA is present in the unfertilized egg cytoplasm is clear. That it has been in existence there for some considerable time in untranslated form is not proven, but is nevertheless very likely.

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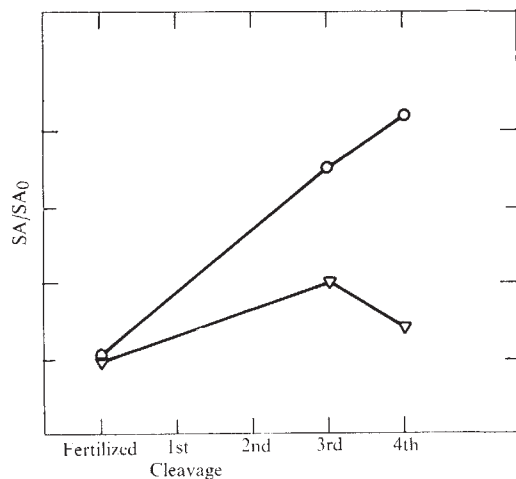


Fig. 5 Changes in relative specific activity of microtubule proteins and total soluble proteins during early cleavage of *Arbacia*. Specific activity (SA) of microtubule proteins at various cleavage stages calculated as described in Fig. 3 is related to the specific activity of microtubule protein labelled in the 30 min interval starting at fertilization (SA₀). Specific activities (SA) of 150,000g soluble proteins (c.p.m. mg $^{-1}$ protein) are also related to (SA₀) for soluble proteins. Actinomycin D was present at $20 \mu\text{g ml}^{-1}$. Microtubule proteins (○) and total soluble proteins (▽).

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LETTERS TO NATURE

PHYSICAL SCIENCES

Detection of Water Cluster Ions at the High Latitude Summer Mesopause

A SOUNDING rocket was launched recently from the Andöya range (69° 17' N), chiefly to study the ion composition around the cold summer mesopause, and its relation to ambient temperature, ionization production and ionization loss rates. The most striking result was the large size of the water cluster ions detected and the extremely rapid change in the ion composition around 85 km. The rocket, a Nike Cajun launched on August 8, 1971, at 1211 GMT, reached an altitude of 98.6 km and carried the following experiments.

(i) A quadrupole mass spectrometer surrounded by a liquid helium cryopump which scanned the positive ion mass spectrum 10 to 140 a.m.u. in periods of 1.76 s. Positive ions were drawn to a circular electrode biased to -15 V with respect to the rocket body, and some of the ions passed through a hole in the centre of the electrode into the mass analyser. The ion beam was accelerated to the front end of a channel electron multiplier whose output was monitored. Similar methods have been used in previous measurements of the mesospheric ion composition^{1,2}.

(ii) Two identical, spherically screened electrostatic probes deployed on booms were used to make measurements of total positive and negative charge³.

(iii) The ambient temperature was determined by an array of ionization chambers which measured the intensity of solar Ly α as a function of height. In the atmosphere Ly α is chiefly absorbed by molecular oxygen, so its intensity is inversely proportional to the amount of molecular oxygen overhead. An analysis of the radiation intensity yields the atmospheric scale height, which is proportional to the atmospheric temperature (a technique used successfully by J. E. Hall, private communication).

(iv) The payload was to be launched in quiet daytime conditions, but a Geiger-Müller detector sensitive to electrons with energies greater than 20 keV and protons greater than 300 keV was included to monitor possible background precipitation.

(v) Three radio receivers were used for the measurement of electron density and collision frequency from Faraday rotation and absorption measurements on 1.3, 3.8, and 7.8 MHz signals transmitted to the rocket from the ground.

The solar zenith angle at the time of launch was 55°. Ground based observations using a 27 MHz riometer and an H magnetometer indicated almost quiet ionospheric conditions, but the experiment showed that a weak particle precipitation event was in progress in the region of the rocket trajectory. This precipitation dominated the ion pair production both on the up and down legs of the flight. Fig. 1 shows the ambient temperature in the height range 70 to 90 km, with a minimum of about 150 K at roughly 85 km.

Ions were detected by the mass spectrometer between a height of 70.7 km on the up leg and one of 69.8 km on the down leg, with water cluster ions $\text{H}^+(\text{H}_2\text{O})_n$ dominating the composition below 84 km on both legs. Clusters of higher order were found with increasing height until an abrupt

cutoff was reached at 84.5 to 86.0 km. Simultaneously, meta ions appeared (chiefly Mg^+ and Fe^+) and NO^+ and O_2^+ emerged as the dominating species. The only exception to the cutoff of water cluster ions was H_3O^+ , which was detected in diminishing quantities up to 87.5 km. The ion 48^+ , identified as $\text{NO}^+\text{H}_2\text{O}$, was also detected to higher altitudes.

The largest cluster ion found on the up leg was 109 a.m.u., corresponding to $\text{H}^+(\text{H}_2\text{O})_6$, detected in one spectrum taken at 84.5 km. On the down leg, the largest cluster ion detected was 91 a.m.u. ($\text{H}^+(\text{H}_2\text{O})_5$), in three spectra between 85.9 and 82.2 km.

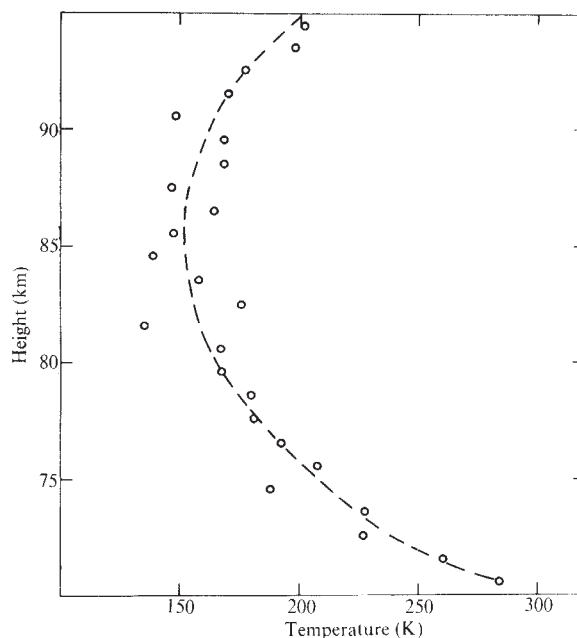


Fig. 1 Ambient temperature as measured with Lyman alpha technique.

It is striking that such large clusters are present and that there is a rapid change in ion composition around 85 km. This change is accompanied by a steep increase in total ion and electron densities. Because the ion production function derived from the particle flux varied only slightly around 85 km, we deduce that the enhancement in the charge distribution resulted from a reduction in the recombination efficiency of the dominant ions.

Results obtained on the up leg are summarized in Fig. 2. The mass peaks were identified by their centre positions. Although the low resolution of the instrument produced peaks up to 2.5 a.m.u. wide in the low mass range and 6 a.m.u. in the high mass range, the central positions of clearly defined and often repeated peaks showed standard deviations of only 0.5 a.m.u. Calibration of the instrument in the laboratory showed that it was accurate in determining the masses of rare gases up to Xe. But because the heaviest cluster ions appear only in a few scans, we have assigned them an uncer-

tainty of ± 1 a.m.u. Because we expected that $\text{H}^+(\text{H}_2\text{O})_n$ ions would represent the "terminal" ions in the upper mesosphere, and these are separated by increments of 18 a.m.u., we made no attempt to achieve high mass resolution, preferring to concentrate on sensitivity at the high mass range. Metal ions in the range 23 to 28 a.m.u. were not resolved, and the peaks at 30^+ and 32^+ , corresponding to NO^+ and O_2^+ respectively, are shown as one double peak. The final sensitivity calibration showed an increase by a factor of 2 from N_2 (28 a.m.u.) to Xe (128 to 136 a.m.u.); these measurements were not corrected for possible differences in electron multiplier efficiencies. Typically, an ion current of 10^{-10} A to the orifice electrode corresponds to 10^3 pulses in the N_2 peak.

appearance of metal ions, chiefly 24^+ and 56^+ ; the main Mg and Fe isotopes. A possible contribution to the 56^+ peak from 55^+ cannot be excluded, but is rather unlikely in view of the disappearance of 37^+ and 73^+ . The 30^+ and 32^+ peaks are here by far the dominating species. While the 32^+ exceeds the 30^+ at all altitudes in the cluster ion region, the 30^+ exceeds the 32^+ peak above this level. This transition is also taking place between the third and fourth scans shown in Fig. 2. The probe current in Fig. 2 shows minima between 84.7 and 85.2 km, and the electron profile exhibits a somewhat broader minimum around the same level. Both the probe current and the electron density show sharp increases above the minima.

The height variation of the effective recombination coefficient

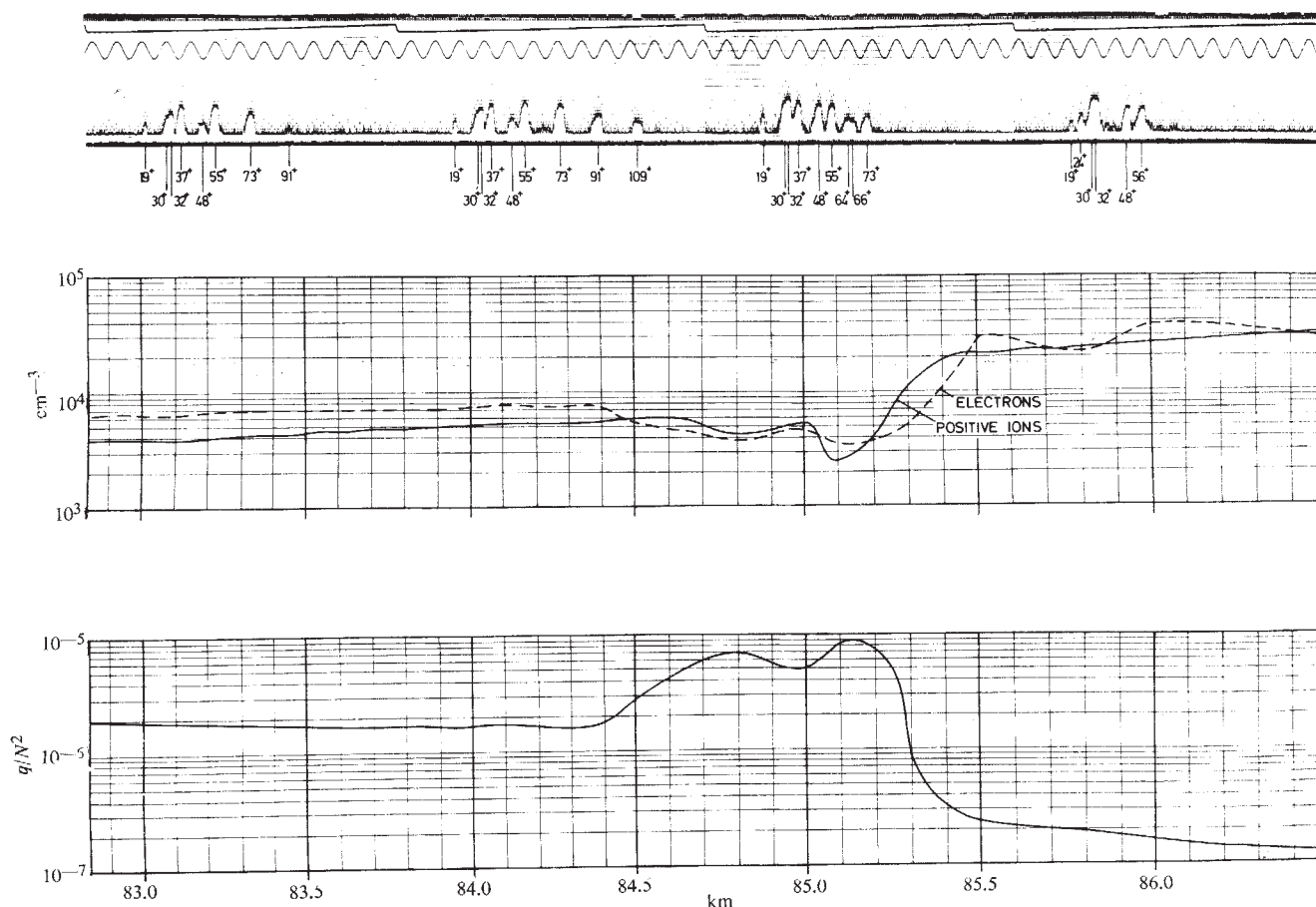


Fig. 2 A summary of results obtained on the up leg through this transition region. The upper part of the figure shows telemetry records of the mass spectra. Also shown are the positive ion densities determined by the electrostatic probes, the electron density as derived from the Faraday rotation experiment and the effective recombination coefficient, defined as $\alpha_{\text{eff}} = q/N^2$, where q is the ion production rate and N is the electron density. The mass spectra shown are not actual ion currents but the output of a free-running 16-step logarithmic scaler operating on the pulses from the ion detecting channel electron multiplier. Arrival of 2^n pulses in the scaler results in a 1 ms output pulse of amplitude corresponding to the n th level. The 0–5 V telemetry format is linearly divided in sixteen levels corresponding to the 2^1 – 2^{16} scalings. Thus the number of counts arriving in any time interval can be determined with a precision in time of less than 2 ms. The 1 ms duration of the level voltages prevents the signal from receding below a level where the repetition period of the scaler levels is less than 1 ms. This results in an overall picture of the mass peaks resembling that from a logarithmic current representation.

The heaviest ion detected, 109 ± 1 a.m.u., appears in the second scan of Fig. 2. In the third scan, the ion population of water clusters is shifted to lower order, the 91^+ and 109^+ peaks no longer being detected and 30^+ and 32^+ emerging as the dominant species. The 48^+ peak, which is here increased at least ten-fold, we identify as $\text{NO}^+\text{H}_2\text{O}$, and the double humped peak between 55^+ and 73^+ we attribute to the unresolved intermediates O_2^+O_2 and $\text{NO}^+(\text{H}_2\text{O})_2$ at 64^+ and 66^+ , respectively. There is a dramatic change in composition between the time of the third scan and the time of the fourth scan, a period corresponding to a height difference of 0.9 km.

The fourth scan shows the disappearance of all water cluster ions except 19^+ and a trace of 37^+ and the simultaneous

shown in Fig. 2 is based on the measured electron and ion densities and the ion production rate derived from the particle counter. Starting at 83 km, α_{eff} shows a slight decrease with height to 84 km, then an increase to a maximum between 84.5 and 85.3 km followed by a sharp decrease to a low value at 85.5 km. The values shown contain uncertainties in the electron density determination, in the computational procedure of deriving the ion production rate from only one particle counter, and in the geometrical factor of that counter.

It is seen that the sharp decrease in α_{eff} is simultaneous with the disappearance of most cluster ions and that the change appears to take place in only 200 or 300 m.

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Is Polyoxymethylene a Cosmopolymer?

AMONG interstellar polyatomic molecules, formaldehyde is now second only to ammonia in the spectroscopic certainty of its identification. Unlike some of these molecules, for example, ammonia and water, formaldehyde has been detected in many different regions of our Galaxy. This has led to the speculation that its occurrence is a general feature of the spiral arms of the Milky Way¹. If this speculation is correct then the chemical reactions of this molecule under interstellar conditions are of considerable relevance to discussions of the chemical evolution of our Galaxy.

In the laboratory, one of the more interesting chemical reactions of formaldehyde is its facile polymerization to linear macromolecules of high molecular weight (10^3 – 10^6 a.m.u.) and having a predominantly polyoxymethylene chain structure². One is prompted therefore to ask the question: can formaldehyde react in a similar way in the dense, cold clouds of the interstellar medium to form the rodlike helical macromolecules formed at ambient temperatures and pressures? In other words, is polyoxymethylene a cosmopolymer? As a first approach to this question I examine here the thermodynamic stability of polyoxymethylene under the conditions thought to prevail in the clouds of the interstellar medium.

The polymerization of formaldehyde can be mediated by a number of initiators including γ and X-rays, and occurs in the gas, liquid and solid phases. The reaction is a chain reaction and proceeds by ionic mechanism either through carbonium ion or oxanion chain carriers. The polymer so produced is known to occur in two crystalline modifications: (i) hexagonal, space group P_3 , ($a=4.46$ Å; $c=17.3$ Å; $\rho=1.49$ g cm⁻³); and (ii) orthorhombic, P_{2121} , ($a=4.77$ Å; $b=7.65$ Å; $c=3.56$ Å; $\rho=1.52$ g cm⁻³ (ref. 3). In both crystalline modifications the macromolecular chains are helical, parallel to the c -axis and differ only in the pitch of the helix. The equilibrium between formaldehyde and its polymer is now well understood and the partial pressure of monomer, p , can be expressed in terms of temperature by an expression of the form⁴

$$\log(p, \text{ kNm}^{-2}) = -(3.453 \pm 0.054) \times 10^3/T + (10.81 \pm 0.15) \quad (1)$$

With few exceptions, polymerization processes are exothermic and exentropic, and are thus subject to the restriction that, at

a given monomer concentration, polymerization will not occur if a critical "ceiling" temperature, given by equation (1), is exceeded. Alternatively, at a given temperature there is a minimum monomer concentration, defined by (1), which must be exceeded before polymerization may occur. For the purposes of this discussion, the equilibrium pressure is expressed as a number density in the temperature range 10–200 K (Table 1).

Table 1 Number Density of Monomeric Formaldehyde in Equilibrium with Polyoxymethylene

T (deg. K)	N (molecules cm ⁻³)
10	$10^{-31.5}$
20	$10^{-14.3}$
30	$10^{-8.5}$
40	$10^{-5.8}$
50	$10^{-4.0}$
60	$10^{-2.9}$
70	$10^{-2.1}$
80	$10^{-1.5}$
90	$10^{-1.0}$
100	$10^{-0.6}$
120	1
150	10^{+6}
200	10^{+11}

The heat capacity of solid, crystalline polyoxymethylene has been measured in the temperature range 10–300 K⁵ and, together with the heat of combustion of the polymer⁶, provides a satisfactory order of magnitude check on the values in Table 1. It must be emphasized that Table 1 is based on an extrapolation of equation (1) over a wide temperature range which ignores the phase changes of the monomer. This is not a serious limitation because it only reduces the precision with which the "ceiling" temperature is defined for a given number density of formaldehyde. For the present purpose the precision obtained (± 5 K) is adequate.

Estimates of the column densities of formaldehyde in the hundred or more sources observed to date lie in the range 10^{12} – 10^{15} cm⁻² (ref. 7). Assuming an average column length of 1 kpc yields an estimated range of 10^{-6} – 10^{-9} cm⁻³ for the average number density of formaldehyde in the interstellar medium. It is clear from Table 1 that at temperatures below the mean galactic temperature (100 K) the abundance of monomeric formaldehyde in some regions may exceed the "thermodynamic limit" required for polymerization.

The interesting temperature range is 50–100 K (HI regions). In this temperature range it is not unrealistic to expect chemical reactions to occur at a rate consistent with the time scale (10^2 – 10^8 yr) on which interstellar chemical processes occur⁸. In many discussions of interstellar chemistry the ubiquitous but poorly understood interstellar grains are invoked as one plausible locus for complex chemical reactions. There is also a highly controversial literature on the nature of the grains themselves. Linear macromolecules of the type discussed above may conceivably constitute one type of grain constituent and polymerization may be one nucleation mechanism for their formation. Clearly, a detailed examination of these suggestions would be a worthwhile contribution to our understanding of chemical evolution.

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Maximum Entropy Power Spectrum of Long Period Geomagnetic Reversals

CRAIN *et al.*¹ computed a power spectrum of the proportions of normal polarity measurements during the Phanerozoic, and their results were used as parameters for a stochastic model for geomagnetic reversals². New data presented by McElhinny³ warrant a re-examination of the power spectrum of reversals during the Phanerozoic. Whereas Crain *et al.*¹ used a hanning window in an attempt to minimize the end effects of the short record, a radically different approach, proposed by Burg⁴, is used in this note. The purpose of this letter is to point out the existence of a powerful new method for the analysis of short records.

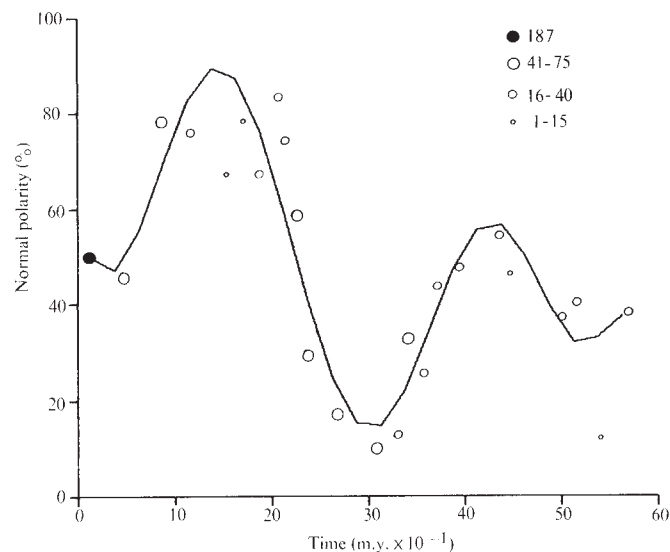


Fig. 1 Percentage of normal polarity in world-wide palaeomagnetic investigations for the Phanerozoic. (Data from McElhinny³. Number of observations as shown by symbols.)

The computation of a power spectrum using either the periodogram (Jones⁵) or the autocorrelation technique of Blackman and Tukey⁶ requires an assumption about the extension of the data outside their available range. Thus, the periodogram method assumes a periodic extension of the data, with one period being equal to the length of the data, whereas the autocorrelation technique assumes a null extension to the data. Both these assumptions are particularly unrealistic for short segments of data. Indeed, as shown by Toman⁷, truncation of records may result in substantial frequency shifts in the computed spectrum. Burg⁴ has proposed a spectral method, known as the maximum entropy (ME) method, which is based on the information or entropy content of the data. The significance of this technique is that it does not require an assumption about the data outside the available range. Further, as shown by Lacoss (unpublished work), the spectral window depends on the data being analysed and considerable improvement in resolution over conventional methods is achieved. Ulrych (unpublished work) has shown that the frequency shifts, mentioned above, which result from short truncation lengths may be obviated by use of the ME method.

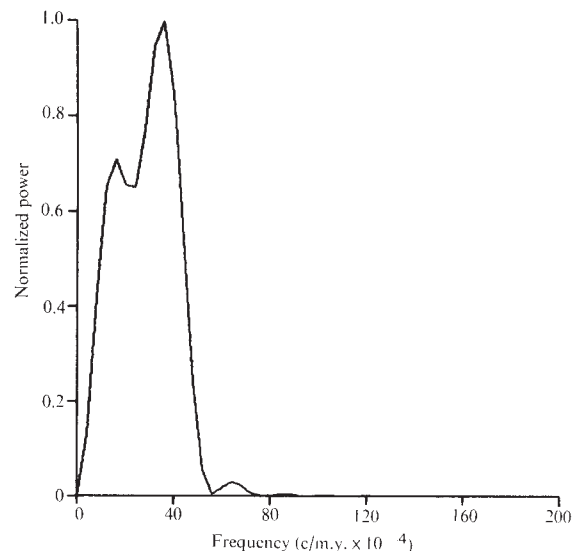


Fig. 2 Power spectrum computed as the square of the modules of the Fourier transform. Sampling interval, 25 m.y.

The ME power estimator may be written in matrix form (Lacoss, unpublished work) as

$$P_E = p \Delta / E \Gamma^* \Gamma E^*$$

where $\Gamma = \text{col}(1, \gamma_1, \gamma_2, \dots, \gamma_{N-1})$, $E = \text{col}(1, e^{i\lambda}, e^{i2\lambda}, \dots, e^{i(N-1)\lambda})$, $\Delta = \text{sampling interval}$, p and the γ_i are obtained, as suggested by Burg⁴, by an iterative solution of the equation

$$R \Gamma^* = P$$

where $P = \text{col}(p, o, o, \dots, o)$ and R is the $N \times N$ correlation matrix of the process.

To apply the Burg ME method to the data of McElhinny³ I have fitted a ninth order polynomial to these data by means of orthogonal polynomials and interpolated with a sampling interval of 25 m.y. In the fitting process, each point was assigned a weight equal to the number of corresponding observations. The interval chosen is the average interval of the McElhinny data, and corresponds to a Nyquist period of 50 m.y.

A finer sampling interval will not alter the spectral resolution. It alters the Nyquist frequency and the interval Δf in the frequency domain. The spectral resolution is governed by the length of record and, for the normal intervals of power

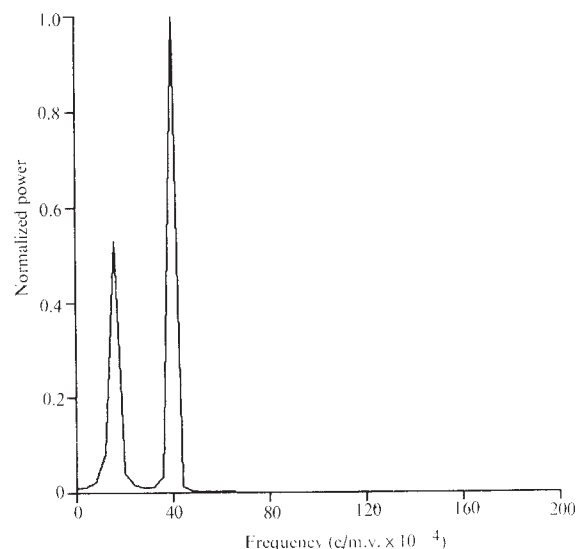


Fig. 3 Maximum entropy power spectrum. Sampling interval, 25 m.y.

estimation, by the spectral window. Using this new technique the window adjusts itself to the data.

Fig. 1 shows the ninth order polynomial fit to the percentage of normal polarity observed in world-wide palaeomagnetic investigations for the Phanerozoic. The Fourier power spectrum computed without tapering of the data is shown in Fig. 2 and the Burg ME spectrum is illustrated in Fig. 3.

The existence of the spectral maximum suggested in Fig. 2 is clearly demonstrated by the ME spectrum. It is apparent that the geomagnetic field in the Phanerozoic exhibits a periodicity of 700 ± 100 m.y. and 250 ± 50 m.y. It has been suggested by Crain *et al.*¹ that the shorter variation may be correlated with the 280 m.y. rotation of the Milky Way. The longer period variation has not been previously reported.

The present analysis does not, of course, preclude the existence of the 75 m.y. period found by Crain *et al.*¹. I do not believe, however, that the data justify a higher order fit.

As pointed out by Crain *et al.* it is impossible to perform a rigorous error analysis. Various orders of polynomial, different weightings and sampling intervals, however, led to the error bounds quoted above.

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New High-strength Stainless Steels

A COMMON method of producing high creep strength in metals is to introduce a second, dispersed, phase to act as an obstacle to the motion of dislocations. At large volume fractions of the second phase this simple method gives very large increases in strength. Another important feature of high-temperature alloys, however, is that their strength should be retained for the duration of their service life, and this implies that the second phase particles must be resistant to coarsening. This is a very stringent condition and the most effective way of

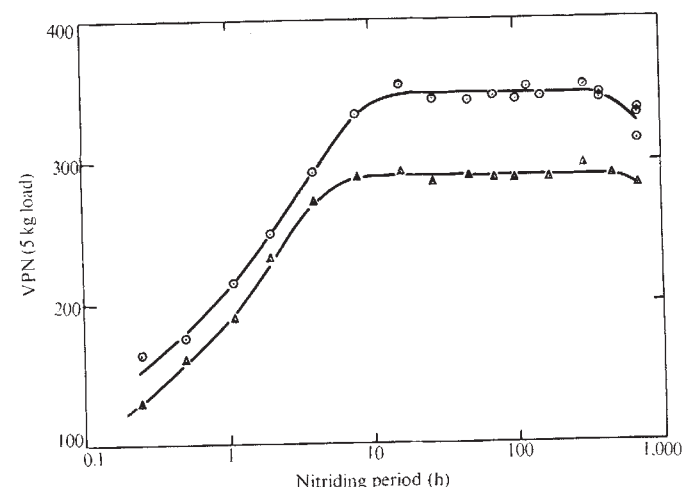


Fig. 1 The variation of room temperature Vickers hardness (Vickers Pyramid Number) with nitriding period at 1,050°C. ○, 1.5 Ti; △, 0.5 Ti.

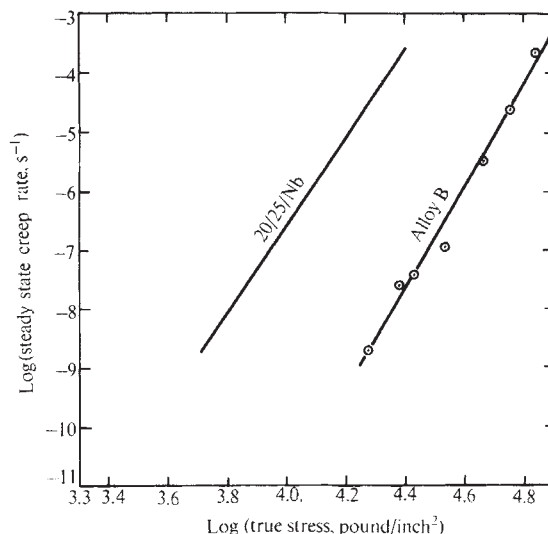


Fig. 2 A comparison of the creep strength of the nitrided alloy (alloy B nitrided 16 h, 1,050°C) with the matrix material.

meeting it seems to be to use a dispersed phase with a very large negative free energy of formation. This is the basis of alloys such as sintered aluminium powder (SAP) and thoria dispersed nickel (TD nickel).

The alloys discussed here are based on an austenitic stainless steel containing a dispersion of titanium nitride (TiN). This compound has a large negative free energy of formation and is much more stable than the other dispersed phases occurring in the steel. The alloy may be formed by the diffusion of nitrogen into a steel containing titanium in solution, the subsequent reaction producing a dispersion of TiN. This process of preferential nitriding has been used previously, for example, by Mukherjee and Martin^{1,2} on Mo/Ti and Mo/Zr alloys and by Spears *et al.*³ on ferritic steels; a discussion on nitrogen diffusion kinetics in austenitic steels containing titanium has been given by Kindlimann and Ansell⁴.

Table 1 Initial Compositions of the Alloys

Alloy	Cr	Ni	Ti	C	Nb	Wt % Si	Mn	B	Fe
A	20.3	25.0	0.48	0.007	0.12	0.05	0.41	<0.001	Balance
B	19.6	24.6	1.53	0.009	0.10	0.05	0.42	<0.001	Balance

The initial compositions of the steels used are given in Table 1. They were supplied by BISRA (The Corporate Laboratories of the British Steel Corporation) as 0.025 inch thick strip from which tensile creep specimens of gauge section 1×0.25 inch were stamped. The alloys were nitrided in pure, dry nitrogen at 1 atmosphere pressure at 1,050°C. The variation of room temperature Vickers hardness with nitriding time is shown in Fig. 1. Clearly a marked increase in hardness occurred in both alloys, reaching a maximum in 10–16 h which corresponded to the production of a uniformly hardened structure. This level of hardness was maintained for nitriding periods up to ~300 h and supports the original postulate of good long term stability of strength. The higher hardness obtained in the steel containing initially 1.5 wt % Ti is consistent with the formation of a larger volume fraction of dispersed phase.

An indication of the very large improvements obtained in creep strength is given in Fig. 2 which plots the secondary creep rate obtained at a given stress for the 1.5 wt % Ti alloy nitrided for 16 h at 1,050°C. Also shown for comparison is the line representing the behaviour of conventional niobium stabilized 20 Cr/25 Ni steel. At a given stress, the creep rate is reduced by $\sim 10^4$ over the matrix material and this consti-

tutes a most significant improvement. The ductility obtained, as measured by the strain to the onset of tertiary creep, was typically within the range 2–6% which is satisfactory for alloys of this strength.

The data presented here are the preliminary results of a programme aimed at assessing the suitability of the alloys for fuel element cladding in nuclear reactors.

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Nature of Quickclays

SMALLEY¹ recently disagreed with an old paper of mine². This paper was in fact a translation of a still older publication³ which was written originally in Norwegian. Smalley ignores the rather extensive Scandinavian literature on the problem since that time. A summary of these results can be found in a more recent publication⁴ in which the development from the first crude attempts in 1946 to modern colloidal-chemical viewpoints is stressed.

At the end of his contribution Smalley states "In mineralogical terms, however, quickclays are not really clays at all". This statement needs some qualification. The essential point about the quickclays is that they contain non-swelling clay minerals such as illite, chlorite and vermiculite, but not montmorillonite. The fact that many quickclays have rather a high silt content is due to the higher permeability of silt-bearing than non silt-bearing clays, and thus the probability of a change in the chemistry of the water phase is greater in the coarse varieties. There are also, however, quickclays containing more than 80% particles finer than 2 μ m, mainly of illitic nature.

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Reply to Rosenqvist

PROFESSOR ROSENQVIST has, to a certain extent, missed the point of my note¹. His famous 1953 paper² was cited, rather than some of the more recent Norwegian publications, simply because it is a key paper in the development of quickclay investigations. It, rather than any previous or subsequent papers, introduced into the field of geotechnology the idea of ion leaching leading to quickness. I appreciate that much subsequent work has been done but the basic idea is still held to be valid by most workers in the field and shapes much current thinking on quickclays.

The Rosenqvist approach still puts the emphasis on clay minerals and colloid chemical factors as being responsible for the characteristic properties of quickclays. I wished to suggest that possibly this was not the best approach and that it may be the hitherto neglected non-clay mineral fraction which is

responsible for quickness. This proposal was stimulated by the results of Pusch and Arnold³ who found it impossible to leach a clay mineral soil to quickness, suggesting that the clay mineral content of a soil may not be the critical part. It must be realized that in many quickclays the so-called clay fraction (<2 μ m) contains an appreciable proportion of non-clay mineral particles. And, as regards terminology, if the non-clay mineral fraction forms the bulk of a soil material and determines its properties it is perhaps illogical to refer to that material as a clay.

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BIOLOGICAL SCIENCES

Lung Cancer as an Endocrine Disease

EVERY cigarette smoker does not develop lung cancer and so factors other than smoking must determine whether or not this disease develops. I have been investigating the possibility that hormones are involved in the development of lung cancer, and have measured the content of individual and total 17-oxosteroids and total 17-hydroxycorticosteroids (17-OHCs) in the urine of patients and controls. I found that patients with lung cancer excreted less androsterone (3 α -hydroxy-5 α -androstan-17-one), compared with its 5 β -isomer aetiocholanolone, and more 17-OHCs than normal subjects¹. Low androsterone excretion in patients with lung cancer had been reported before². The mean ratios of androsterone to aetiocholanolone and of androsterone to 17-OHCs in eighty-four patients were significantly ($P < 0.00001$) lower than those of 100 normal men and of fifty-two control patients with chest diseases other than lung cancer (hospital controls). In fact the ratio of 17-OHCs to androsterone can be used as a diagnostic test for lung cancer with an accuracy of about 90% (Fig. 1). When the differences between cancer patients and controls were combined by linear discriminant analysis¹, more than 90% of patients had negative discriminant scores whereas more than 90% of normal men had positive scores.

Thus the association between steroid abnormalities and lung cancer is sufficiently high to be of diagnostic value. This association merits comparison with the association between cigarette smoking and lung cancer because of the aetiological significance attached to the latter association. Table 1 gives the smoking habits of lung cancer patients and controls as percentages of the total number in each group.

There was a significant difference in the number of non-smokers in the normal control group compared with the lung cancer group (χ^2 test), but no significant difference in the

Table 1 Smoking Habits of Lung Cancer Patients and Controls

	Lung cancer (84)	Hospital controls (88)	Normal men (100)
Non-smokers	0	2.2	18.0
Cigarettes: 1–14/day	32.2	38.4	28.0
„ 15–24/day	43.3	39.3	36.0
„ 25+ /day	24.5	22.1	18.0

Figures are expressed as percentages of total numbers in each group. Numbers in parentheses denote the total number of subjects in each group. Pipe smokers are included with cigarette smokers in this table. One gram of pipe tobacco has been considered equivalent to one cigarette.

distribution of the categories of smokers between any of the groups. Thus, the association with cigarette smoking and lung cancer is far less significant than that with steroid abnormalities. It would of course be rash to ascribe any aetiological significance to a biochemical parameter, however significantly it is associated with lung cancer, because this association could be an effect of cancer. Various chemical abnormalities are well known in cancer patients and in the metabolism of tumours *in vitro*³. Furthermore, steroid excretion is known to be influenced by various factors, such as physical or emotional stress, including acute illness⁴. Chronic illness, particularly associated with malnutrition and loss of weight, results in a general decrease in the excretion of 17-oxosteroids and 17-OHcs⁵. The question of cause or effect is particularly important because in rare cases lung tumours excrete polypeptides with adrenocorticotrophic hormone (ACTH)-like activity. This applies to less than 1% of all lung cancer cases⁶, and can be disregarded as a cause of the steroid abnormalities found in most lung cancer patients in the present study. Second, surgical removal of lung tumours from forty-five lung cancer patients showed that steroid abnormalities are not consequences of the presence of the tumours. Surgical resection of lung tumours which are known to secrete ACTH-like polypeptides results in a prompt return of the 17-OHcs to normal concentrations⁷. In my study, however, steroid abnormalities did not disappear after removal of the lung tumours and it can be concluded that these abnormalities are not the effects of the presence of the lung tumours.

The criticism that the steroid abnormalities are due to debilitating illness can also be answered in the case of lung cancer. The excretion of total 17-oxosteroids, or of one of the two quantitatively major 11-deoxy-17-oxosteroids, aetiocholanolone, is not lower in lung cancer than in controls. The excretion of androsterone but not its 5 β -isomer aetiocholanolone is low in lung cancer. In fact, the excretion of the latter steroid is significantly higher in lung cancer compared with hospital controls¹. It would be difficult to explain why the excretion of only androsterone and not that of aetiocholanolone is lowered as a result of debilitating illness, and only in lung cancer patients

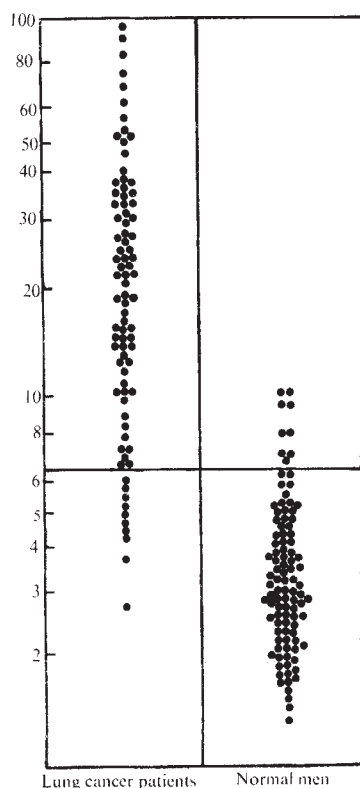


Fig. 1 Steroid excretion in lung cancer patients and normal men. Androsterone and 17-OHcs are expressed in mg/g creatinine/l. The horizontal line at a ratio of 6.3 gives the best separation between cancer patients and controls.

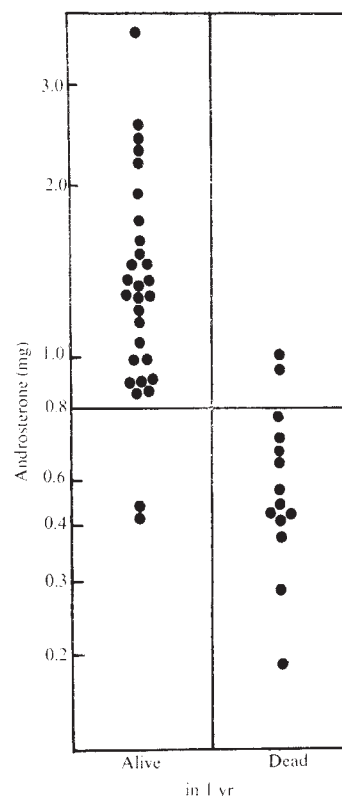


Fig. 2 One-year survival in surgically treated lung cancer patients. The horizontal line at an androsterone value of 0.8 mg gives the best separation between those who died within one year and those alive 1 yr after resection.

and not in patients with other chronic chest diseases. In addition, most of the lung cancer patients reported here were studied during the first few days in hospital for investigation of chest complaints, and in most cases before a diagnosis of lung cancer was established, and they had suffered no significant weight loss¹. Since androsterone is an anabolic steroid⁸, debility is more likely to be due to a deficiency of this steroid, which is not an effect of debilitating illness.

Further evidence of the significance of androsterone and other steroids in lung cancer comes from the very significant correlation between the length of survival and the concentrations of androsterone, aetiocholanolone and 17-OHcs in patients whether their tumours were removed or not⁹. The preoperative levels of androsterone alone can be used to predict very accurately one year survival in lung cancer patients whose tumours were removed by surgical resection. Of forty-two cancer patients who underwent surgical treatment, fourteen died within a year. Out of the fourteen, twelve had less than 0.8 mg of androsterone/g creatinine/l., whereas twenty-six out of those twenty-eight alive had androsterone concentrations higher than this value (Fig. 2).

Such a close correlation of the levels of androsterone with length of survival cannot be dismissed lightly as the effect of illness, but it could reflect only the stage of the disease and need not be of aetiological significance. My results, however, show that the concentrations of androsterone are not correlated with the stage of the disease. Thus, there was no significant difference in the mean amounts of androsterone excreted between fifty patients in the surgically treated group (in which the disease is considered to be at an early stage), on the one hand, and the eighty-four patients in the group with inoperable lung cancer (which is usually considered to be at an advanced stage of the disease), on the other (1.22 ± 0.84 mg and 0.99 ± 0.70 mg respectively). It therefore seems that the excretion of androsterone is not related to the stage of illness, but to the resistance of the patients to the growth and spread of the tumour.

Information available on the physiological effects of androsterone and other steroids suggests that these steroids are involved in defence mechanisms against the growth of tumours. These steroids have potent effects on the metabolic rate, cortisol being catabolic and androsterone being anabolic. A high 17-OHcs/androsterone ratio may thus result in increased catabolism and may lead to cachexia seen in many patients in the advanced stage of this disease. It is well known that corticosteroids affect the immune response, which is known to play an important part in the spread of tumours. It has also been shown that the establishment of blood-borne metastasis requires the matrix of a fibrin-clot, and fibrinolysis by streptokinases results in a decrease of blood-borne metastasis¹⁰. Androsterone is known to increase fibrinolysis, and a deficiency of this steroid might facilitate blood-borne metastasis. A high oestrogen/androgen ratio is known to favour the establishment of chemically-induced tumours¹¹, and it is perhaps of significance that lung cancer patients excrete more oestrogens¹² and less androsterone than controls.

Finally, since the deficiency of androsterone is associated with poor prognosis in lung cancer, correction of this deficiency by the administration of this steroid or a suitable precursor might be of therapeutic value. Such a clinical trial would provide a conclusive answer to the question of the involvement of steroid hormones in the aetiology of lung cancer.

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Hormonal Interrelations in Beef Cows with Induced Multiple Ovulations

ALTHOUGH there is wide interest in hormonal induction of multiple births in cattle¹, it is not possible to induce two or three ovulations reliably. Further advances will require a better understanding of the patterns of hormone concentrations during follicle growth. This report describes peripheral plasma concentrations of oestrogens, progesterone and luteinizing hormone (LH) during the 96 h before induced oestrus and multiple ovulations.

Eight beef cows with calves 80–100 days old were injected intramuscularly every 2 days with 100 mg of progesterone in corn oil for eight to ten injections. On the day of the final progesterone injection (day 0), each cow received 2,000 IU of pregnant mare serum gonadotrophin (PMS; Ayerst Laboratories) subcutaneously at 0900 h. Calves were weaned from pairs of cows selected at random on days -2, 0, 2, and 4 to determine the effect on the ovarian response (oestrus and

Table 1 Effect of Weaning and Progesterone-PMS on Ovarian Function in Groups of Two Beef Cows

Group	Calves weaned*	Day of oestrus	No. of CL	Progesterone trough†	Hormonal patterns over 96 h before oestrus†			
					Oestrogen peak§		LH peak¶	
1	Day -2	5	1	96 h	48 h	13 pg	None	—
2	Day 0	4	1	96 h	24 h	11 pg	12 h	3.6 ng
		4	9	48 h	60 h	51 pg	24 h	2.7 ng
3	Day 2	3	2	24 h	36 h	32 pg	12 h	9.0 ng
		4	6	36 h	24 h	28 pg	36 h	5.7 ng
4	Day 4	4	3	48 h	72 h	20 pg	24 h	4.1 ng
		4	10	24 h	24 h	22 pg	72 h	4.2 ng
		4	11	36 h	36 h	24 pg	60 h	4.7 ng

* On day 0, PMS and last dose of progesterone were injected.

† Measured from onset of oestrus backwards.

‡ Progesterone concentrations less than 1.5 ng/ml.

§ Length of period when oestrogen concentrations were elevated, and highest level.

¶ Length of period when LH concentrations were elevated, and highest level.

numbers of ovulations) of progesterone/PMS-treated cows.

From day 0 to the onset of oestrus, blood was collected from each cow at 0600 h and 1800 h into heparinized tubes. After centrifugation, plasma was collected and stored at -20° C for hormone assay. A bull was used to detect oestrus.

All calves were weaned on the same day (October 20, 1970) to eliminate temporal effects on cow behaviour. Five to ten days after oestrus, each cow was laparotomized and the number of corpora lutea and follicles were noted. We assumed that the number of corpora lutea reflected the number of follicles that had reached maturity and ovulated.

Plasma progesterone was assayed using the competitive protein-binding assay² and LH was determined by the double antibody radioimmunoassay³. Antiserum against bovine LH (B-225, supplied by Dr G. Niswender) was used at a dilution of 1:120,000. Purified LH (LER-1072-2, supplied by Dr L. E. Reichert, jun.) had a potency of 1.66 NIH-LH-SI U/mg. Total plasma oestrogen concentration was determined by radioimmunoassay⁴. Oestradiol-17 β -6,7-³H, with a specific activity of 40 Ci/mmol, was used and antiserum was supplied by Dr B. V. Caldwell.

The interval from PMS injection to onset of oestrus was 4 days in six cows and 3 and 5 days in two cows (Table 1). The time that the cows were weaned relative to day 0 influenced the number of corpora lutea. Weaning calves two days before the end of hormonal treatment (group 1) restricted follicular growth to only one follicle, which ovulated. When calves were weaned four days after hormonal treatment (which coincided with the day of oestrus), follicular development was considerable, and most follicles had ovulated (group 4). In the remaining groups, a variable number of follicles ovulated, and it was observed at laparotomy that many follicles greater than 10 mm diameter had been induced to grow but had not ovulated. The hormone data for one cow from each of groups 1 and 4 are given in Fig. 1. Other animals in these groups gave similar results. Cows in groups 2 and 3 gave intermediate results.

As Table 1 shows, progesterone concentrations declined to below threshold levels (1.5 ng/ml., referred to as a trough) in groups 2, 3 and 4 by 24 to 48 h before oestrus. In group 1, however, progesterone had declined to threshold levels on the day of the last progesterone injection. Thus weaning stress influenced the progesterone levels since they were 2–4 ng/ml. at the same time in other cows.

Oestrogen concentrations increased to a maximum or near maximum level on the day before oestrus in all cows. Oestrogen peak height was greater in groups 2, 3, and 4 than in group 1. A regression analysis of plasma oestrogen indicated that the slopes of the regression lines for those cows having multiple ovulations were homogeneous and were steeper than for the group having single ovulations ($P < 0.01$). In a previous study, by Hancock *et al.*⁵, in which urinary oestrene excretion was measured for

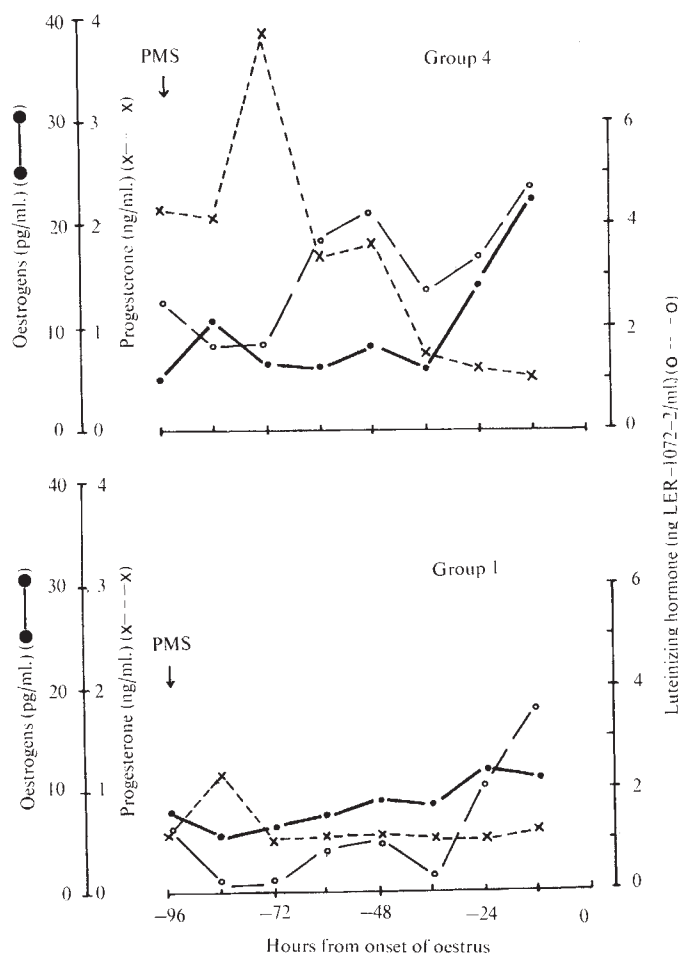


Fig. 1 Oestrogen, progesterone, and luteinizing hormone concentrations in plasma during the 96 h before oestrus in a progesterone-PMS treated cow from groups 1 and 4.

several days while human menopausal gonadotrophin was administered to women, the regression of the log of 24 h urinary oestrone excretion over time was steepest in patients with multiple conceptions.

A reciprocal relationship existed between oestrogen and progesterone levels in all cows. Plasma oestrogen levels began to increase only after progesterone levels had decreased to below threshold levels. But the timing of the oestrogen increase relative to the beginning of the trough of progesterone was not the same in all cases.

Plasma LH concentrations exceeded 1 ng/ml. before oestrus. Unlike previous studies² in which LH rarely exceeded 1 ng/ml. during pro-oestrus in untreated cows, peaks of LH occurred in all but one cow. It is not known whether the peaks increased to higher levels early in oestrus. There was clear relation between the number of ovulations and the lengths of the period that LH remained above what is considered normal levels (<1 ng/ml.). In group 1 there was a slight increase in LH 12 h before oestrus in only one cow, but LH levels were elevated for 60 to 72 h in group 4.

Thus, time of weaning relative to gonadotrophin injection affected ovulation number and plasma hormone patterns. Multiple ovulations were accompanied by higher plasma oestrogen and LH levels.

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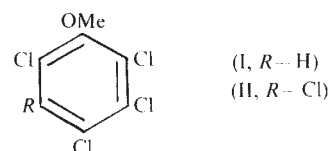
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2,3,4,6-Tetrachloroanisole Association with Musty Taint in Chickens and Microbiological Formation

A "MUSTY" taint in chicken eggs has been attributed to the presence of 2,3,4,6-tetrachloroanisole (I) in litter shavings by Engel, de Groot and Weurman¹, who showed that the feeding of small amounts of this compound to chickens caused a musty taint in both eggs and broiler meat. The samples of shavings that contained 2,3,4,6-tetrachloroanisole (I) also contained pentachloroanisole (II). Following recent occurrences of musty taint in the UK broiler industry, we have examined chicken carcasses and broiler house litter for the presence of chloroanisoles and investigated their origin.



Samples of chicken tissue and of litter were extracted with pentane in a modified Likens² still, and the extracts were examined by gas chromatography. Tissue samples from tainted birds contained up to 8×10^{-2} μg of (I) and 2×10^{-2} μg of (II) per g of fresh tissue. The highest concentrations were found in skin and depot fat with approximately 3% of these levels in breast muscle. Chickens containing even these low amounts were considered inedible when tested by taste panels after cooking, so that some sensory assessment of these compounds appeared desirable. Odour thresholds determined on the vapour above aqueous solutions of various chloroanisoles revealed a wide range including some remarkably low concentrations (Table 1).

Table 1 Detection Thresholds for Chloroanisoles in Aqueous Solution

Compound	Threshold concentration (in $\mu\text{g g}^{-1}$ solution)
Pentachloroanisole	4×10^{-3}
2,3,4,6-Tetrachloroanisole	4×10^{-6}
2,4,6-Trichloroanisole	3×10^{-8}
2,3,6-Trichloroanisole	3×10^{-10}

Tests were made with twenty-three subjects in triplicate and are significant at the 1% level.

Samples of litter from a broiler house producing tainted birds contained both (I) and (II) at levels up to 7 and 5 $\mu\text{g g}^{-1}$ respectively. Birds with the highest levels of 2,3,4,6-tetrachloroanisole in the fatty tissue and the highest sensory ratings for mustiness were obtained from those areas of the house which contained the highest levels of chloroanisoles in the litter. Chloroanisoles were apparently entering the chickens from the litter where they were present in relatively high concentration. The mode of entry has not yet been established.

No chloroanisoles were found in any of several samples of fresh shavings and sawdust. Pentachlorophenol and 2,3,4,6-tetrachlorophenol, however, are applied extensively to freshly sawn timber as antifungal agents and we have found these compounds (up to 40 and 100 $\mu\text{g g}^{-1}$ respectively) in several samples of shavings and sawdust produced from imported timber. The presence of these chlorophenols in shavings suggested that the chloroanisoles might arise through microbiological methylation in the litter.

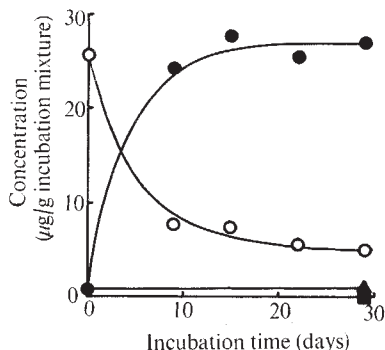


Fig. 1 Conversion of 2,3,4,6-tetrachlorophenol to 2,3,4,6-tetrachloroanisole in simulated litter. Replicate cultures were incubated aerobically at 25° C in closed containers of 300 ml. capacity and whole cultures taken for analysis at the times indicated. The complete system contained 22.5 g of sawdust, 10 ml. of water, 833 and 201 μg of 2,3,4,6-tetrachlorophenol and pentachlorophenol respectively, and 2.5 g of tainted litter as inoculum. ○, 2,3,4,6-Tetrachlorophenol in complete system; ●, 2,3,4,6-tetrachloroanisole in complete system; ▲, 2,3,4,6-tetrachloroanisole in autoclaved complete system and in system without phenol; ■, 2,3,4,6-tetrachloroanisole in system without inoculum.

Accordingly, "simulated litter" experiments were set up in which a small inoculum of tainted litter was incubated with sawdust, 2,3,4,6-tetrachlorophenol and pentachlorophenol. There was a virtually quantitative conversion of the 2,3,4,6-tetrachlorophenol to (I) within 9 days (Fig. 1); formation of (I) was negligible when the inoculum or the tetrachlorophenol was omitted. The ability to effect these conversions could be transferred through serial cultures using small inocula but was destroyed by autoclaving and was therefore attributed to microbiological action. A similar but incomplete conversion of pentachlorophenol to (II) was observed (50% conversion after 29 days). Examination of the fungal flora of the original tainted litter and of the simulated litter cultures showed that the predominant organisms were *Aspergillus sydowi*, *Scopulariopsis brevicaulis* and an unidentified species of *Penicillium*. Tests with pure isolates of each of these organisms growing in defined medium or in sawdust litter showed them to be capable of converting both 2,3,4,6-tetrachlorophenol and pentachlorophenol to the corresponding anisoles. A. J. Cserjesi (private communication) has also shown that a similar conversion is effected by a *Trichoderma* species previously shown to degrade pentachlorophenol³.

These results have implications beyond the immediate context of our experiments. First, the sensory activity of certain of the chloroanisoles is remarkable, and they produce "musty" or "earthy" taints in extremely low concentrations. This is true of few known compounds, and is more generally associated with metabolic products of Actinomycetes^{4,5}. Second, the occurrence of traces of toxic chemicals originally added to wood as preservatives presents potential hazards when shavings and other products from such wood are used in situations involving foodstuffs. Further complications may arise when such compounds undergo chemical or microbiological conversions *in situ*.

In this case the extremely low sensory thresholds of the chloroanisoles, and of (I) in particular, are fortunate because they probably discourage the consumption of chickens con-

taining these compounds, the toxicities of which have not yet been established.

A detailed account of this work will be published elsewhere.

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Photoinduced Free Radicals of Visual Pigments in Solutions mobile at -196° C

IN rigid solutions of visual pigments stabilized for studies of electron spin resonance (ESR) at the temperature of liquid nitrogen white irradiation creates free radicals with resonance patterns consisting of broad singlets¹. We have obtained more refined information by providing solvents mobile at these low temperatures and by irradiation of the visual pigments with selected monochromatic beams rather than with white light.

We used mixtures of liquid propane and propene condensed at low temperatures from the gaseous state to examine the retinals. Because the possibility has been raised^{3,4} that the first stage in the photochemistry of vision is mediated by the Schiff base composed of phosphatidyl ethanol amine (PEA) and 11-*cis*-retinal², an analogue of this base, PEA-all-*trans*-retinal, was examined for free radical formation in the same mixed solvent.

All-*trans*-retinal (grade S VI, Sigma) was recrystallized from petroleum ether at -78° C³; 9-*cis*-retinal and 3-*cis*-retinal (Sigma) were not further purified. PEA, chromatographically pure (General Biochemical Corporation), was stored at -20° C in evacuated vials. PEA-all-*trans*-retinal was prepared as reported² with some modifications. It was further purified from the initial reagents by chromatography on a silica column in complete absence of oxygen and moisture in a pre-flamed, highly evacuated glass line.

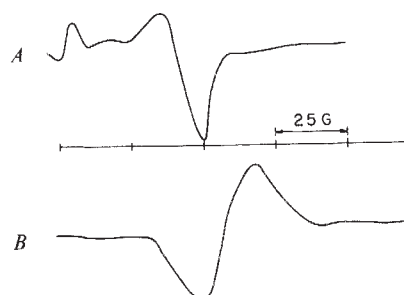


Fig. 1 A, ESR signal of either all-*trans*-, 9-*cis*- or 13-*cis*-retinals. B, ESR signal of bleached retinals.

The mixed solvents propane and propene (2:1 v/v) used for ESR and optical studies were purified in a vacuum line by distillation from -78°C to -196°C . The solutions of the pigments were prepared in a vacuum line in a combined tube consisting of silica tubing (3 mm outer diameter) for ESR measurements fused in line to a silica cell (10 mm square cross-section) for optical spectroscopy. The recrystallized solute was added to the cell, which was thoroughly evacuated, before the mixed solvent was condensed at -196°C . After the tube had been sealed off at the cylindrical end, the temperature was raised to -78°C to hasten solution. The retinals readily dissolved in concentrations beyond the needs of the experiments, and the solutions remained clear and homogeneous when cooled to -196°C . PEA-all-*trans*-retinal could be brought adequately into solution only by raising the temperature to -50°C . Unlike the other pigments, some would precipitate out of solution in about 0.5 h at liquid nitrogen temperature. All the samples were irradiated uniformly at -196°C in a silica dewar with a monochromatized beam (500 mm monochromator, Bausch and Lomb Company) from a high pressure mercury arc (BH-6, General Electric Company). ESR and optical absorption spectra were taken alternately after pouring the solution from one end to the other merely by inverting the combined cell under liquid nitrogen. Optical spectra were measured at this temperature with a Cary 14 spectrophotometer and the ESR spectra with a Varian ESR spectrometer model V4502.

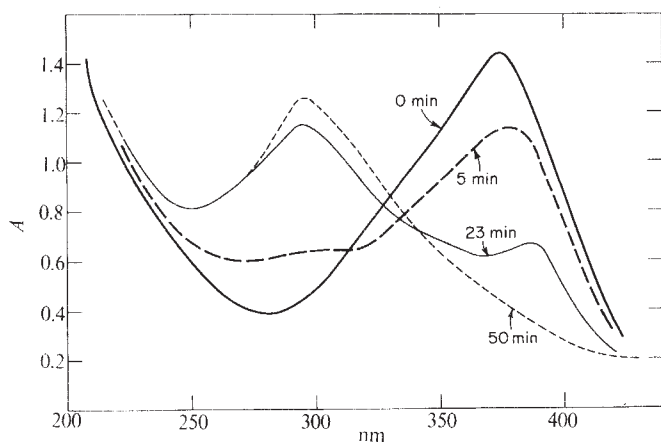


Fig. 2 Absorption spectra at -196°C of all-*trans*-retinal and of its photochemical products, upon irradiation for various times at 370 nm.

The solutions were transferred for mixing without exposure to air by means of a glass siphon tube surrounded by liquid nitrogen.

On irradiation with a narrow slit (bands 1.7 nm wide) ranging over the spectrum from 330 nm to 390 nm, all-*trans*-retinal quickly produced a complex unsymmetrical ESR signal (Fig. 1A). Continued irradiation with this beam at 370 nm for about 2 h effected little, if any, change in the shape of the optical absorption spectrum. But when the irradiation band was widened to 6.8 nm, the maximum shifted from 370 nm to longer wavelengths, decreasing in magnitude until the entire band was bleached (Fig. 2). Concurrently, a new band emerged with a maximum at 290 nm. These spectral changes could not be reversed by further irradiation at the new maximum (290 nm) nor by raising the temperature to -78°C , in contrast to the results obtained by Jurkowitz⁵ from pigment dissolved in organic glasses at -196°C . Further irradiation at 290 nm, however, gave rise in succession to other maxima that eventually stabilized in one at 260 nm.

During the spectral changes induced by irradiation at the fixed wavelength (370 nm) the shape of the ESR signal remained unchanged. When, however, the wavelength of the irradiation was set at the absorption maximum (290 nm)

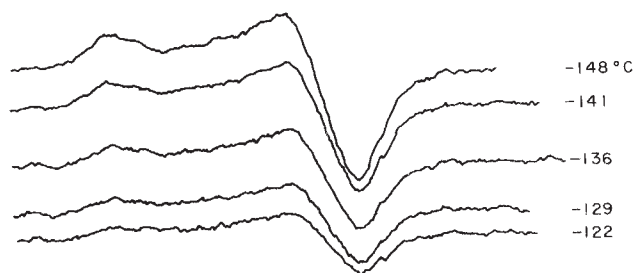


Fig. 3 Changes in ESR signal with change in temperature of irradiated all-*trans*-retinal. Increasing temperatures downward. Note little change in shape despite changes in intensity.

characteristic of the bleached all-*trans*-retinal, the complex unsymmetrical ESR signal broadened, lost structure, and ended in a singlet similar to the one reported by Grady and Borg (Fig. 1B). The absorption spectrum of the bleached retinal extends into the region transmitted by the glass optics used by Grady and Borg. The asymmetric ESR signal when expressed as a second derivative of intensity with respect to field strength (or frequency) shows (Fig. 4) two closely spaced components of roughly equal intensity and a third component at lower field strengths. As the temperature of the sample increases (Fig. 3), the intensity seems to lessen without appreciable change in the shape of the signal.

9-*cis*-retinal and 13-*cis*-retinal, when irradiated at the wavelengths of their optical maxima, exhibited optical and ESR changes analogous to those of all-*trans*-retinal. But the times of irradiation required for induction of observable changes in optical spectra were decidedly longer than the quick responses to irradiation observed in all-*trans*-retinal.

The free radicals formed by photolysis of all-*trans*-retinal were fairly stable when maintained at -196°C in the dark, with some loss in the signal intensity after several days. With gradual increase in temperature, particularly above -140°C , the intensity of the ESR pattern lessened, giving no indication of the sharpening expected from the considerable reduction in viscosity (Fig. 3). Similarly, no appreciable sharpening in the spin spectrum accompanied the reduction in viscosity at -196°C engendered by the addition of methane to the solution until it constituted about 15% of the solvent. At -78°C the ESR signal disappeared but the photoinduced changes in the optical spectrum effected at -196°C persisted.

The following electron-transfer experiment illustrates how mobile solutions of free radicals at liquid nitrogen temperature can function as reagents in solution chemistry. An irradiated

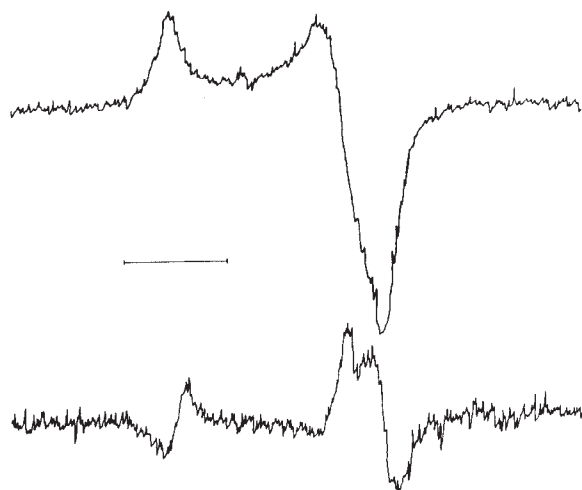


Fig. 4 Second derivative of ESR signal of irradiated all-*trans*-retinal under first derivative of signal. It shows three components two of which at right are almost of equal intensity.

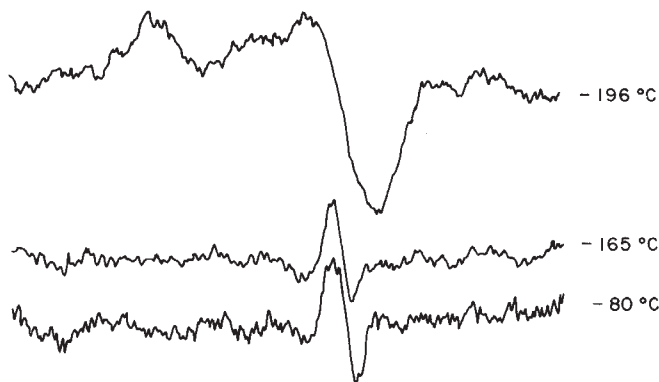


Fig. 5 Electron transfer reaction between irradiated all-*trans*-retinal (signal, above) and electron acceptor, tetrachloroparaquinone (signals, below).

solution of all-*trans*-retinal was transferred at -196°C into the solution of chloranil (tetrachloroparaquinone) in the same solvent by means of the transfer tube. The ESR signal of chloranil, a well known electron acceptor, was easily distinguishable from that of the retinal. After the transfer, the ESR signal of the mixed solution held in the dark was due only to retinal. The solution after being set aside for 3 days was irradiated once more to increase the intensity of the signal.

Again only the asymmetrical ESR spectrum of the retinal was observable. The temperature of the solution was then raised to -165°C , whereupon it was found that the narrower simple signal of chloranil had completely replaced the complex signal of the retinal (Fig. 5). The electron-transfer reactions had evidently required activation energy thermally available between -196°C and -165°C . The signal from chloranil is about as sharp at -165°C as at -80°C in a solution of much reduced viscosity.

PEA-all-*trans* retinal could not be irradiated for as long as the half hour in which precipitation occurs at -196°C . Irradiations of 5 min, however, had been sufficient to produce easily detectable variations in the absorption spectrum of all-*trans*-retinal and had produced its ESR signals, although in these conditions no detectable ESR signal appeared from the Schiff base nor were changes in its absorption spectrum observed.

Because the complex asymmetrical signal is generated on irradiation of all-*trans*-retinal at its optical absorption maximum, the free radicals giving rise to the ESR pattern must arise from its photochemical product. The broad symmetrical ESR singlet produced by irradiating the "bleached" all-*trans*-retinal at its optical absorption maximum indicates that the signal reported by Grady and Borg has its origin in a secondary reaction. Similar phenomena are also characteristic of 9-*cis*-retinal and 13-*cis*-retinal. But the long irradiation required for the appearance of the optical changes from the *cis* forms suggests that during the induction period these substances are first transformed to a common intermediate, possibly the *trans*-retinal itself.

The shape of the asymmetric signal is the same in different conditions and persists as the temperature is raised until its intensity virtually vanishes (Fig. 3). We conclude that one species of free radicals is present, for several species would be expected to anneal out at different temperatures. From the second derivative of the ESR signal (Fig. 5), it is inferred that the three components constitute one signal and that the envelope is consistent with near axial symmetry of the g tensor. This interpretation implies that the molecular tumbling by the solvent molecules at the low temperatures is not sufficient to average out the ESR response even though considerable reduction in viscosity was achieved by raising the temperature from -196°C to -120°C and also by adding 15% methane to the solvent. On the other hand, the ESR signal of the chloranil (Fig. 5) consists of rather sharp structure scarcely changing

between -165°C and -80°C where the solvent is very fluid. The molecular asymmetry of the chloranil is known to be less marked than those of the retinals. Grady and Borg never observed the asymmetric ESR signal when the all-*trans*-retinal was dissolved in a rigid matrix. Possibly because of the cage effect the free radicals were rapidly combined with dissociated fragments or electrons and did not build up a sufficient concentration to be observed, in contrast to the more stable free radicals arising from the bleached retinal.

The marked contrast in the effectiveness of the narrow (1.7 nm) and of the broad (6.8 nm) spectral beams with maximum at 370 nm in the phototransformation of all-*trans*-retinal suggests that two successive quanta of small time interval may be required for the transformation of the all-*trans*-retinal into the bleached retinal.

With regard to the electron transfer reactions in solution it should be noted that solutions mobile at -196°C are not restricted to solutes of low polarity such as the retinals, because solvents for wide varieties of inorganic and organic solutes can be prepared that are homogeneous and mobile at the low temperatures⁵, and consequently free radicals derived from these may be studied in solutions mobile at these and even lower temperatures.

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Quinacrine Mustard Fluorescence of Sex Chromatin in Human Amniotic Fluid Cell Cultures

SINCE the work of Zech¹, a fluorescent staining technique has been used for identification of the Y chromosome in the interphase nuclei of cells from human male subjects. No recognizable fluorescence of the Barr body or sex chromatin mass has been observed in the nuclei of uncultured human amniotic fluid cells from female foetuses obtained by amniocentesis.

We now report that the sex chromatin body in the interphase nuclei of growing amniotic fluid fibroblast cultures, unlike uncultured cells, does show a distinct fluorescence, so that sex identification can be made unambiguously by use of the fluorescent staining method. The selective binding of quinacrine mustard to the distal portion of the long arm of the Y chromosome and the lack of specific binding to one of the X chromosomes in the normal female led other investigators² to assume that a difference exists between the heterochromatin of the X (inactivated X) and the Y at the "physicochemical" level. Our results together with the findings of Greensher *et al.*³ on the fluorescence of sex chromatin seem to refute this assumption.

using the oil immersion objective fitted with a diaphragm for light control. The percentage of cell nuclei with fluorescing sex chromatin bodies was recorded for each sample. Photographs of representative cells were taken with the fluorescent microscope. The same cells were then restained either with Feulgen or with thionin⁵, and were rephotographed with the same magnification using ordinary light.

We found that the sex chromatin body in the nuclei of fibroblast cultures from female foetuses could be clearly identified by the distinct fluorescence, peripheral location and typical shape in most of the cells (Fig. 1a). Seven of eleven specimens were unambiguously identified as females and four as males by their characteristic fluorescent bodies.

Table 1 Fluorescing Sex Chromatin and Y Body in Amniotic Fluid Fibroblast Cultures

Case No.:	1	2	3	4	5	6	7	8	9	10	11
% Fluorescent sex chromatin body *	40.6	34.4	41.4	0	72.2	0	74.1	47.5	60.5	0	0
% Sex chromatin body after thionin staining	78.1	60.9	78.9	0	80.9	0	86.2	60.8	67.9	0	0
% Fluorescing Y body	0	0	0	78.7	0	75.1	0	0	0	73.5	84.9
% Polyploid cells as determined by excess sex chromatin body count	14.0	4.3	3.6	11.7	25.9	14.3	31.2	21.8	19.1	16.2	16.8
Identified sex (by karyotype analysis)	F	F	F	M	F	M	F	F	F	M	M

F, Female; M, male. * Values represent the mean of two or three samples examined for each case.

Fibroblast cultures from eleven pregnant women were derived from samples of amniotic fluid obtained by amniocentesis before therapeutic abortion from the sixteenth to twenty-fifth week of gestation. The cultures were trypsinized and plated directly on microscope slides in Leighton tubes in McCoy's 5a medium with 20% foetal calf serum. After growth for 24 h the cells were rinsed in saline solution, fixed in acetic acid-methanol (1:3) for 0.5 h and air dried. The cells were then kept in MacIlvain's citric acid-phosphate buffer (pH 4.1) for 5 min and air dried. Drops of freshly prepared solution of quinacrine mustard (QM) at a concentration of 100 µg/ml. in distilled water were then placed on slides to cover the cells completely. The cells were stained for 5 min, rinsed in water and mounted in buffer. Some cells were also stained for 20 min in QM solution at a concentration of 50 µg/ml. in phosphate buffer (pH 7.0) as recommended by Caspersson *et al.*⁴. The slides were then examined under a Leitz Ortholux photomicroscope with a Ploem vertical ultraviolet illuminator and standard fluorescence filters. All observations were made

Karyotypes were prepared from all the fibroblast cultures and in each instance the sex chromosome constitution confirmed the results of the fluorescent study. The percentage of nuclei with fluorescent Barr bodies varied from 34–74% (Table 1), depending on the cell density; the value increased with increase in cell density. A close correlation was observed between the morphology of the fluorescent Barr bodies and the sex chromatin masses in thionin or Feulgen-stained preparations in each of the nuclei of a majority of the cells (Fig. 1b). But the overall frequency of fluorescent Barr bodies in cells from the seven female foetuses was consistently lower than that found in the same cells after thionin staining, indicating, perhaps, a lesser specificity of QM over thionin in its binding capacity to sex chromatin. Most of the cells had one fluorescent body, but 4–31% showed two or four Barr bodies in each nucleus (Fig. 3a and b). The nuclei were larger in cross-sectional area with two or four Barr bodies, and were presumably produced by the fusion of two (tetraploid) or four (octoploid) diploid nuclei or by endomitosis. This observation is in

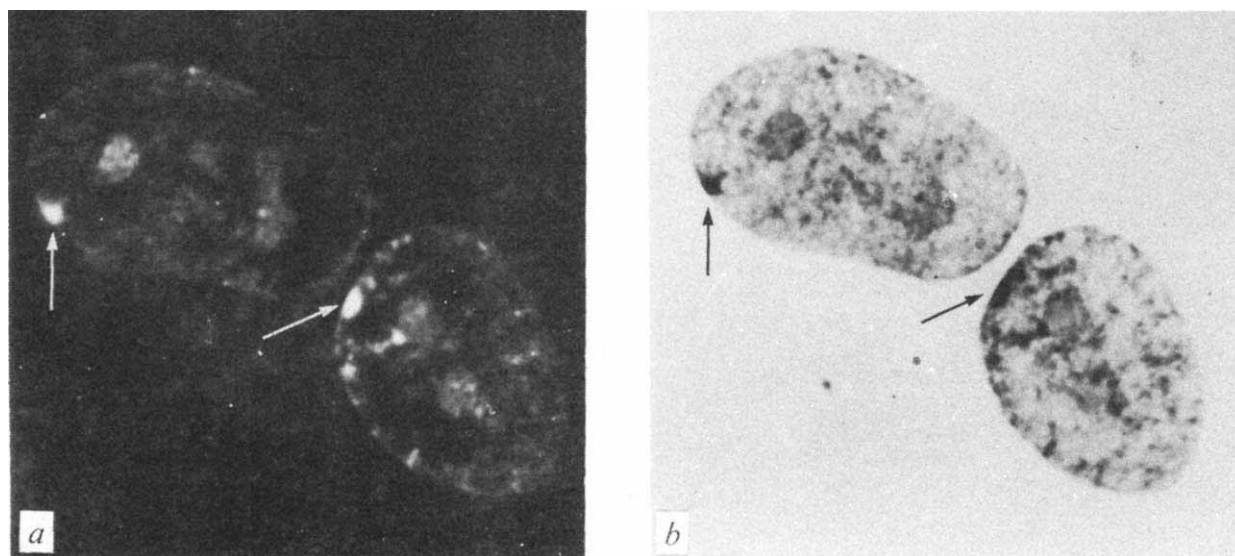


Fig. 1 a, Diploid nuclei from amniotic fluid fibroblasts showing a distinctly fluorescing sex chromatin body (arrow) ($\times c. 5,000$). b, Diploid nuclei after being stained with thionin. Note the correspondence of the Barr and fluorescing body (arrow).

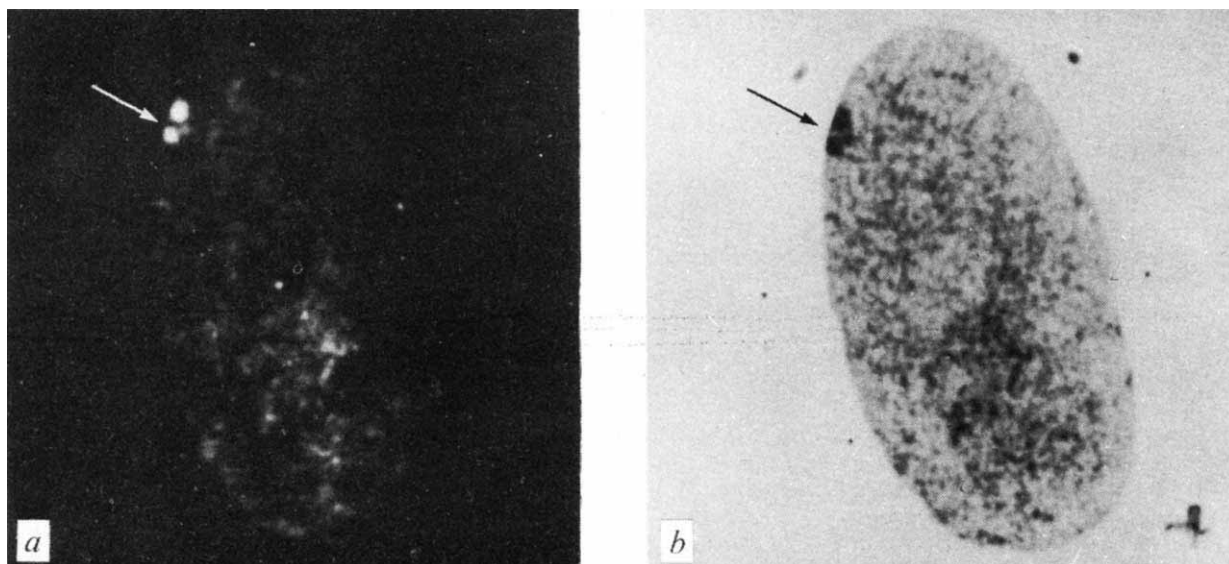


Fig. 2 *a*, A presumptive tetraploid nucleus with two fluorescing Barr bodies (arrow) ($\times c. 5,000$). *b*, Same nucleus after being stained with thionin (arrow).

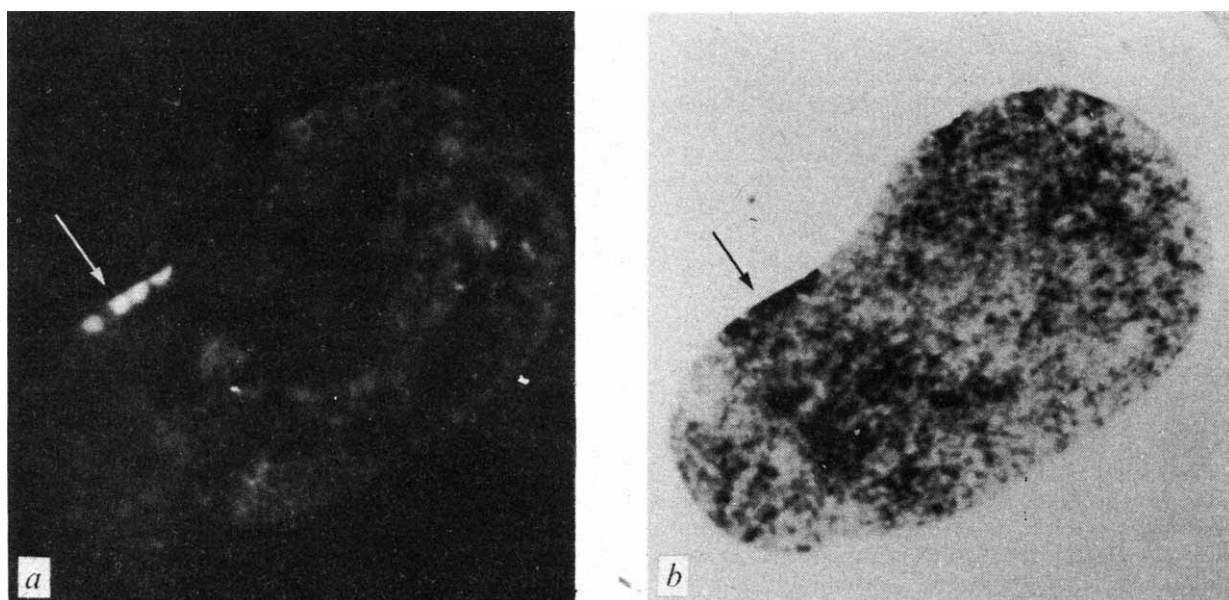


Fig. 3 *a*, A presumptive octoploid nucleus with four fluorescing Barr bodies (arrow) ($\times c. 5,000$). *b*, Same nucleus after being stained with thionin (arrow).

agreement with previous reports of an increased frequency of polyploidy in amniotic fluid cells⁶. The fluorescent Barr body was three or four times as large as the Y body of nuclei from male foetuses. In addition to the sex chromatin, some cells had one or two additional small fluorescent bodies presumably originating from the chromosomes 3 and D⁷. The nucleoli also fluoresced but usually not as brightly as the sex chromatin. Although fluorescent bodies were demonstrable with the pH 4.1 and pH 7.0 buffers, they appeared more distinct with the lower pH buffer.

It is clear that the fluorescence of sex chromatin can be detected in certain cell types in certain conditions (such as cultured fibroblasts) whereas it is not demonstrable in other circumstances (such as fresh amniotic fluid cells or cultured leucocytes). The affinity for the fluorochrome may depend on the specific state or property of heterochromatin or reflect certain metabolic conditions of the cell. Quinacrine mustard binding was first believed to have a predilection for the C-G rich regions of DNA by alkylation of guanine. It is now known, however, that other fluorochromes, which lack the alkylating

group of QM, also produce fluorescent bands at the same locations as QM, so the basis for the specificity of this reaction remains unclear. We have observed a progressive decrease in the frequency and intensity of fluorescing Barr bodies after 2–10 min of exposure of cells to a 0.5% solution of trypsin. After removal of the trypsin there is an appreciable increase in the frequency of fluorescent Barr bodies within 3–10 h after resumption of cell growth. When the same cells were stained with thionin no significant change in the frequency of Barr bodies was found. This finding suggests that proteolysis may alter the composition of sex chromatin and that specific proteins as well as DNA may be involved in the binding of these fluorochromes. This observation is in agreement with the findings of Hand⁸ on unfertilized sea urchin eggs. The effects of various agents which inhibit protein synthesis on the fluorescence of sex chromatin and isolated metaphase chromosomes are now being studied and will be reported in detail elsewhere.

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Mercury in Bryophytes (Moss)

RECENT reports in the literature, concerning the ability of certain mosses and lichens to concentrate heavy metals¹⁻³, have led to an investigation of the potential application of mosses as indicators of the transport of mercury through the atmosphere. A number of moss samples were collected to provide information regarding the level of mercury in moss around several types of populated areas. The results reported in this communication are from moss collected within an 80 mile radius of Boston, Massachusetts, along the Maine coast, near the tops of Mount Katahdin in Maine and Mount Washington in New Hampshire, and from Walden, New York, a small town located about 60 miles north of New York City. The data are admittedly limited, but provide sufficient insight into the usefulness of moss as an indicator to warrant the pursuit of a more detailed investigation.

Mosses, as distinguished from vascular plants, have little opportunity to utilize minerals directly from the soil. Minerals are collected through concentrations of the mineral in rain water or are supplied adsorbed to dust. Through the action of the rain or of organic acids, the elementary constituents of the dust particles are released and absorbed by the moss carpet. Since mercury is known to adsorb to most surfaces, it might be expected that dust particles would carry mercury if it were present in the atmosphere. Jaakkola *et al.*¹ have reported the results of analyses for cadmium in the moss *Hylocomium splendens*. Results were presented showing 3-4 p.p.m. in the windward portion of an urban area, while in adjacent areas within 100 km² but further from the urban centre levels were about 1 p.p.m. Results of cation exchange experiments with moss have been reported by Rühling and Tyler^{2,3}. In the case of nickel the process was probably simple passive ion exchange, at least when large amounts of nickel were supplied. For copper, however, the process was not exclusively ion exchange, for only two-thirds of the Cu content could be re-exchanged by repeated leaching with MgCl₂. The sorption and retention of the heavy metals studied followed the order: Cu, Pb > Ni > Co > Zn, Mn. This order was shown to be independent of whether or not the ions were supplied in pure or mixed solutions. The natural carpet of *Hylocomium splendens* exhibited a continuous uptake of Mn, Fe, and Cu from young to old tissues. The "earthy" or mor layer beneath the moss carpet had not enriched the heavy metals above concentrations measured in the old moss tissue.

No measurements of mercury in moss have been reported before. Levels of mercury in soil, however, have been reported to be generally very low. In the Franciscan formation of

Table 1 Distribution of Mercury Levels

Location	Total mercury (in p.p.b.)	Remarks
Cambridge	1,450	Large city
Somerville	1,320	Industrial suburb
Everett	675	Industrial suburb
Lexington	250	Residential suburb
Lynnfield	330	Residential suburb
Danvers	910	Suburban—some industry
Topsfield	286	Rural area
Boxborough	634	Rural area
Chelmsford	465	Residential suburb of Lowell
Billerica	935	Suburb—some industry
Nashua, New Hampshire	1,350	Small industrial city
Walden, New York	2,000	Medium size town concentrated in relatively small area
Damariscotta, Maine	50	Small coastal town
Falmouth, Maine	234	Small coastal town near Portland
Waldoboro, Maine	566	Small coastal town (sample location near large cement plant)
Bath, Maine	< 50	Medium-sized coastal town
Mt Katahdin, Maine	284	High, isolated mountain area
Mt Washington, New Hampshire	< 50	High, isolated mountain area

California, near heavy mercury mining activity, the average levels of mercury in soil are about 100-200 p.p.b.⁴. The geometric mean concentration of mercury in soils of the eastern United States has been reported by the US Geological Survey as 96 p.p.b.⁵. In view of the relatively low values in soil, mercury levels in moss above a concentration of 200 p.p.b. would indicate a potential for use as an indicator mechanism.

Samples from various locations (Table 1) were weighed out and wet ashed using a concentrated nitric acid/sulphuric acid/potassium persulphate digestion procedure. Several samples were refluxed as a cross check on the digestion procedure; results were in close agreement. Each sample consisted of a collection of the green portions of moss tissue removed from the moss carpet. Total mercury was determined using flameless atomic absorption spectrophotometry. Results reported in Table 1 are for dry weight total mercury. The moisture in the moss samples was found to average about 40%, although the sample from Mount Katahdin was 72.5% moisture. This sample was not included in the average. Individual identification of moss types has not yet been completed since so many specimens look alike but are known by different names. Conard⁶ has published a useful guide for this initial survey. The results of the analyses are shown in Table 1. Levels range from 250 to 1,450 p.p.b. in the Boston area, with the Walden, New York, sample recording 2,000 p.p.b. The two mountain samples show low concentrations, as do three of the four samples from locations on the Maine coast. The highest levels in the Boston area were in the samples from Cambridge and Somerville, close to the centre of the metropolitan area. Relatively high readings were also recorded in Billerica, Danvers and Nashua (New Hampshire). These areas have some industrial activity and moderate population size. If mercury was being accumulated as a result of fossil fuel combustion, the relative importance of industrial activity vs. home heating would have to be determined. There is a definite trend towards lower levels in less densely populated areas. An interesting result, however, is that rural areas close to the Boston metropolitan centre generally show higher levels than do coastal areas in Maine with similar population density. The low mercury concentrations on Mount Washington and Mount Katahdin, which are among the highest peaks in New England and are located in remote areas, might indicate that the aeolian path is relatively localized. The one sample from the Maine coast showing greater than 500 p.p.b. was taken near a large cement plant. In this case, the fuel used to fire the kiln would be one possible contributor, although a much more complete investigation is required in this case.

The work described here is preliminary. The mosses need to be classified according to species and age. In addition, the sampling programme should be expanded to include downwind sampling from densely populated and industrial areas. Contour maps of mercury levels can be developed from these types of data. It would be desirable to know more about moss growth in highly industrialized areas. Methods of encouraging the growth of the more hardy varieties need to be developed.

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Possible Biochemical Model for Phenylketonuria

SINCE the demonstration of the primary enzymatic defect in phenylketonuria (PKU) several models have been suggested for this metabolic disorder. No hypothesis, however, has unified the biochemical and clinical characteristics².

Weber *et al.*³ demonstrated an effect of phenylalanine and phenylpyruvic acid (PPA), the two major metabolites found in PKU, on the metabolism of glucose. They observed inhibition by either phenylalanine or PPA of three specific enzymes of glycolysis: hexokinase, pyruvate kinase and 6-phosphogluconate dehydrogenase. On the basis of these data, Weber suggests that phenylalanine and PPA interfere with the biosynthesis of strategic macromolecules in the differentiating brain. He supports this hypothesis by showing that the extent of decreases in the incorporation of radioactively labelled glucose into lipid, RNA and DNA depends on the dose of phenylalanine or PPA. A major shortcoming of the various models is the lack of an adequate explanation of the aetiology of the deficiency in myelin deposition seen in patients. In an attempt to define the causes of the clinical symptoms of PKU, and this deficiency in particular, we have sought preliminary evidence that PPA is the key metabolic factor in PKU.

Homogenates of whole fresh rat brain and liver were prepared in cold 0.25 M sucrose (1 g/10 ml.) and incubated as described previously⁴ to measure the production of ¹⁴CO₂ from ¹⁴C-1-pyruvate. In the first study, both rat brain and rat liver homogenates were used to determine the levels of inhibition by the various metabolites of phenylalanine present in patients with untreated PKU (Table 1).

Of the five metabolites tested, none were significantly inhibitory in the liver, but phenylpyruvic acid (PPA) inhibited

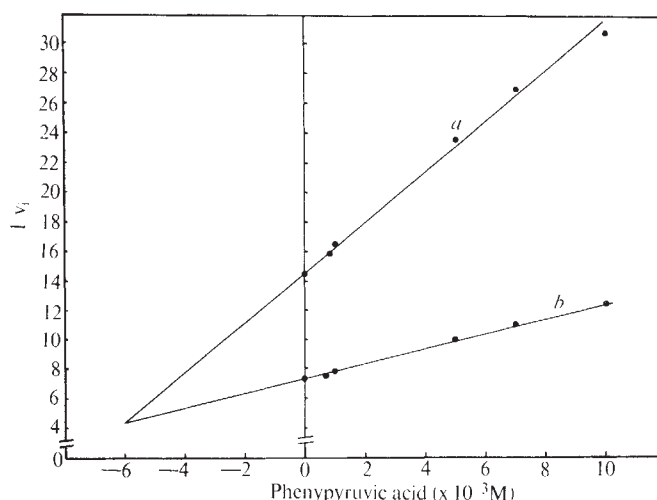


Fig. 1 Effects of PPA on pyruvate decarboxylation. a, Pyruvate 5×10^{-4} M; b, pyruvate 1×10^{-3} M.

pyruvate metabolism in the brain by 50%. We therefore thought it important to determine the type of inhibition exerted by PPA. We measured the effect of various amounts of PPA at two concentrations of pyruvate and plotted the data by the method described by Dixon⁵ (Fig. 1). Clearly PPA is a competitive inhibitor of pyruvate decarboxylation, with a K_i of approximately 6×10^{-3} M in brain homogenate.

These results indicate that, of the metabolites of phenylalanine which accumulate in significant amounts in PKU, only PPA specifically inhibits pyruvate decarboxylation and then only in the brain.

As pyruvate metabolism is central to the energy cycle in adult and developing brain, it is significant that PPA inhibits this important system. We suggest that in PKU an "induced" metabolic block (inhibition) at the site of pyruvate decarboxylation depresses the amount of acetyl-CoA derived from carbohydrate metabolism for energy production through the tricarboxylic acid cycle. Furthermore, a depression in pyruvate metabolism would decrease the amount of acetyl-CoA available for the synthesis of fatty acid and cholesterol which are primary precursors of myelin. This specific site of inhibition coupled with the effects on glycolysis noted by Weber *et al.*³ would starve the brain tissue of energy. Such a condition could be responsible for the depression in synthesis of myelin and myelin precursors, explaining the reduced myelin deposition found concomitant with the mental retardation in PKU. The observation that these phenylalanine metabolites do not inhibit pyruvate decarboxylation in the liver to the same degree as in the brain suggests that other body functions are relatively normal while the brain is starved of energy. Our observations support the hypothesis that PPA inhibition of pyruvate metabolism plays an important role in the aetiology of the mental retardation found in PKU.

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Table 1 Relative Inhibition of Pyruvate Decarboxylation in Rat Liver and Brain Homogenates by Various Metabolites of Phenylalanine

Metabolite added*	Relative activity	
	Brain	Liver
None†	100%	100%
β-Phenylpyruvic acid	53	92
DL-β-Phenyllactic acid	98	94
DL-3-Indolelactic acid	80	84
Indole-3-Acetic acid	84	82
3-Indolepyruvic acid	106	169

* All metabolites at 1×10^{-2} M.

† Homogenates were incubated with 1×10^{-3} M pyruvate for 15 min at 37°C.

BOOK REVIEWS

Aurora

The Optical Aurora. By A. Omholt. Pp. xii+198. (Springer Verlag: Berlin and New York, 1971.) 58DM; \$16.80.

THIS book is the fourth volume in a series on Physics and Chemistry in Space. It is concerned with the detection and interpretation of electromagnetic radiation of wavelengths in the range 100 to 100,000 Å, produced through the interaction between the stream of particles of solar origin and the Earth's atmosphere. In addition, the information concerning this optical radiation is used to deduce the influence of primary particles on the ionosphere and so to examine the perturbations of the ionosphere caused by the particles.

The author explains in his preface that because the subject of his book was very fully treated in Chamberlain's *Physics of the Aurora and Airglow* (Academic Press, 1961), he will concentrate on outlining progress made during the past decade and will refer the reader to Chamberlain's book for relevant background information.

Following an introductory chapter describing auroral forms and morphology, examining the magnetic guidance of particles and defining coordinate systems, there are chapters first on the electron aurora in which data on auroral luminosity are used to study the primary electrons producing the aurora, and second, on the proton aurora, containing a theoretical examination of the characteristics of the hydrogen emission and an account of the information that can be deduced from the observations. The next two chapters deal with the optical spectrum of the aurora (rockets and satellites have extended our knowledge of the spectrum into the ultraviolet and provided more information in the infrared) and the physics of the optical emissions, examining the processes of excitation, the interpretation of the spectrum, the life of metastable oxygen atoms, helium emissions and the sunlit aurora. There follow a review of recent work on temperature determinations from auroral emissions and an analysis of the various forms of pulsing in aurora: pulsating, flaming, flickering and streaming. In a short chapter on the optical aurora and radio observations, the association between the optical aurora and the effects of the enhanced ionization on radio wave propagation is summarized. Finally, the

production and observation of X-rays in aurora are briefly described.

The book is clearly written and well produced and illustrated. It will be useful not only to spectroscopists but to all working in any branch of study of the aurora.

JAMES PATON

Lobachevsky to Pavlov

Science in Russian Culture. By A. Vucinich. Pp. xv+575. (Stanford University, Oxford University: Stanford, California, and London, July 1971.) £8.75.

VUCINICH's second volume on Science in Russian Culture starts with the aftermath of the Russian debacle in the Crimean War. This precipitated passionate demands for social reform, more efficient government, and industrial development. Science was seen as the instrument for their accomplishment, from nihilists who believed that the problem of social organization could be solved only by science, to conservative bureaucrats who saw that science was necessary for better military technique.

The translation of Darwin's *Origin of Species* was published in the year in which the serfs were emancipated. Its effect on the atmosphere of intellectual excitement was profound. In 1862 Turgenev published *Fathers and Sons*, whose hero Bazarov was the prototype of the new man, the scientific son who was to save the land of his fathers. He appeared to be modelled on I. M. Sechenov, the inspirer of Pavlov. While Turgenev was presenting the scientist as saviour, the anti-scientists were denouncing him as the desecrator of the higher moral truth. Prominent among them was Dostoevsky, whose hero in *Notes from the Underground* announced: "The conclusions of reason and arithmetic may be the law of logic, but not the law of humanity." We should "scatter rationalism to the winds . . . send these logarithms to the devil, and . . . live once more by our own foolish will!"

Russian science was strong in mathematics from the time when Euler was installed in the St Petersburg Academy of Sciences. One of the reasons was that reactionary statesmen thought it was too abstract to be politically dangerous. The most characteristic Russian contribution to science was soil

science, founded by Dokuchaev. It was supported both by improving landlords and the Populists who were incensed by the assignment of poor land to the freed peasants. Though chemistry produced Butlerov and Mendeleev, it was retarded by the lack of a chemical industry. Physics was held back for similar reasons.

From 1725 until 1917 presidents of the Academy of Sciences were appointed by the authorities, not elected. The universities were virtually confined to the sons of gentry. Women were excluded and Jews restricted. In 1912 there were 8,000 Russian students studying in Western European universities, about ninety per cent of whom were Jews.

Lobachevsky spent his mathematical life at Kazan, then the most eastern university in Europe. His teacher there was the German mathematician Johann Bartels, who had taught Gauss when he was a boy of twelve. Lobachevsky lectured on his non-Euclidian geometry in 1826. Gauss's appreciation of his work was not published until after Lobachevsky's death in 1856. In 1873 W. K. Clifford, in a lecture at the Royal Institution, compared Lobachevsky with Copernicus. Each had "brought about a revolution in scientific ideas so great that it can only be compared with that wrought by the other". Lobachevsky was not discouraged by lack of mathematical recognition. His practical abilities were appreciated, especially as rector of Kazan University. He was keenly interested in the philosophy of science, and held that it was Bacon who foretold the rise of mathematics as the basis of the new scientific method.

Academician A. N. Krylov, the father-in-law of Kapitza, was an eminent applied mathematician, the translator of Newton's *Principia* with commentaries, and a naval architect who contributed to the scientific foundation of the Soviet Navy. He was related to I. M. Sechenov whom he saw in his boyhood.

A. F. Joffe, being Jewish, found a university career closed to him. After doing notable research under Röntgen the only job he could get was as laboratory assistant in the St Petersburg Polytechnical Institute. He stayed, and ultimately created the school which provided the first generation of Soviet physicists.

Vucinich's comprehensive and readable work is essential for all libraries.

J. G. CROWTHER

Lasers for the Masses

Lasers. By O. S. Heavens. Pp. 159. (Gerald Duckworth: London, September 1971.) £3.25 cloth; £1.25 paper.

The Basic Theory of Lasers and Masers. A Density Matrix Approach. By Jacques Vanier. Pp. xii+115. (Gordon and Breach: New York and London, October 1971.) £4.75 cloth; £2.25 paper.

If it is unfair any longer to describe the laser as a solution searching for a problem, it might not be too unfair to describe many of the books offering to give a general introduction to the laser as answers searching for a questioner.

Unfortunately, Professor Heavens's new book seems to fall into this category. An introduction for the reader "with only a limited knowledge of science", it begins with a brief outline of the nature of light and light sources, and "how things behave when exposed to light". This last covers not only a classical discussion of the properties of reflecting and transmitting media, but also effects in crystals, polarization and the electro-optical effect. There follows a short introduction to quantum phenomena and stimulated emission. These chapters give the impression of a breathless rush around a very wide topic, and one suspects that for the "non-scientific" reader they will raise many more questions than they answer. The sections on lasers are more satisfactory. Perhaps because of delays in publication, however, they tend to devote much more space to ruby and helium-neon lasers than to those such as carbon dioxide and dye systems which may well be more important in the near future. The discussion of the difference between laser and ordinary light is confusing because it runs together ideas about classical coherence and photon counting with the mode structure of the laser beam. The section on applications is surely much too brief for the general reader. Holography is well treated, but cutting and welding, one of the most common topics of interest to lay audiences, is dealt with in a very cursory manner, as are ranging and measurement devices.

This book seems most suitable for that "Abominable Snowman" the educated (and well-off) layman who has the time and inclination to dabble in a little nonmathematical science. Schools may well find the price prohibitive, although the readability of the style makes the book attractive. A final point of importance, if it is intended for school and college use, is that the suggestions for further reading are woefully inadequate and out of date. Obviously, a book of this level would not be expected to give numerous

references to original research, but any reader wishing to follow up a particular topic at a slightly higher level would find Professor Heavens's reading list very unhelpful.

The Basic Theory of Lasers and Masers, in the Documents on Modern Physics series, has a rather misleading title. In fact, this monograph gives a very clear and concise introduction to the density matrix formalism as applied to a range of quantum mechanics problems. Lasers and masers are brought in merely as an illustration of one of the uses of the technique and one is forced to the conclusion that the title was chosen with an eye to salability. With a hard-cover price of £4.75 for a hundred and fifteen pages, the book no doubt needs all the help it can get, but this should not be allowed to detract from its merits.

The density matrix technique, in which an ensemble of identical particles can be described by a unique matrix, is finding wider and wider application in a number of fields of physics. At the moment, perhaps the most interesting area is that of coherent interactions, and this book gives an excellent introduction to the necessary theory. The theoretical level is such as to be accessible to anyone who has gone through a good, present-day undergraduate course in quantum mechanics, and experimental physicists should be able to gain a considerable amount from the analysis and examples. The bibliography has a number of rather surprising omissions, but is adequate.

Both these books have something to offer in the laser field, one at the bottom and the other at the top of the scale of sophistication. However, one must ask how long this spate of beautifully produced but highly priced volumes can continue, especially those which are at best peripheral in value, without the bankruptcy, or at least disillusion in the physics market, of a number of publishers.

D. G. C. JONES

Desert Culture

The Negev: The Challenge of a Desert. By Michael Evenari, Leslie Shanan and Naphtali Tadmor. Pp. x+345. (Harvard University: Cambridge, Massachusetts; Oxford University, London, July 1971.) £7.25.

THE remains of well organized and extensive civilizations in desert regions have provided subjects of study and speculation for well over 100 years. Archaeologists have been foremost in these studies but geographers, agriculturalists and ecologists have also produced their theories on how such elaborate communities have been supported by apparently scanty resources. As far as I know, however, only Pro-

fessor Evenari and his co-workers have attempted to test their hypotheses on the functioning of ancient desert agriculture, by reconstructing the system. Working in the Negev, the authors enlisted the assistance of an archaeologist, geologist, and zoologist, and with generous financial aid from the Ford Foundation, Rockefeller Foundation, the Rothschild Memorial Group and a number of private donors, were able to undertake the necessary studies eventually to reconstruct two ancient farms. The basic surveys that led up to this, the story of the reconstructions and the subsequent scientific work are described in this book.

The result is quite fascinating and, on the basis of carefully collected experimental data, challenges many of the theories previously held about the mode of operation of ancient agricultural systems. For example, one of the most intriguing features of the extensive ancient ruins of the Negev is the occurrence of thousands of stone mounds that are found over the area, often in association with ancient towns. In aerial photographs they show up as an extremely regular feature, often accompanied by gravel strips and in proximity to ancient fields that receive run-off water from the mound and strip-covered slopes. One theory was that they were sites for vine-culture; another, that they might have been connected with dew condensation and water supply. Professor Evenari and his associates reject these hillside-agriculture theories and suggest an explanation in terms of valley agriculture. On the evidence of experimental run-off plots it is shown that clearing the stones and gathering them into mounds increase the annual run-off. This in turn can be utilized for agriculture in the valleys which mainly relies on this source of moisture.

The agricultural results are impressive. Field crops, vegetables, medicinal and pasture plants, as well as a number of orchard crops were grown successfully. The chapters describing this work provide a wealth of information on crop physiology but the subsequent chapters on the adaptation of natural plants to desert conditions contain much information previously published elsewhere.

The authors see the ability of Israel to meet the challenge of its deserts as a measure of its final success and permanence. Not surprisingly the method of management practised by the Bedouin comes in for some criticism. But, if the decline of desert agricultural systems in the past has resulted from exploitation at a higher level than the ecosystem can endure over a long period, perhaps, after all, the nomadism of the Bedouin could represent one well-adapted method of long-term utilization of the desert resource.

M. J. CHADWICK

The columns headed by A show the scores returned by those pupils who had elected to follow a predominantly arts based course to A level, and those headed with an S show the scores returned by those pupils who had elected to follow a predominantly science based course to A level. The original intercorrelations between the adjectives were virtually the same for the A group as they were for the S group, and the factor scores were obtained using the pooled A and S intercorrelation.

The table shows that the A group and the S group agree fairly closely in their estimation of the twelve nouns, with the exception of "men", "English" and "physics". The S group awards "men" a less foolish, a more masculine and a hotter rating. The same group gives "physics" a less foolish, a very much more masculine and a less cold rating than "English" and identifies "physics" more closely with "men". The A group gives "English" a more wise and a less cold rating than "physics", but awards a feminine score to "English" and a masculine score to "physics". The implication seems to be that the A group prefers a somewhat feminine subject to study for A level, while the S group prefers a masculine one.

This feature can be highlighted by listing the difference between the mean factor scores given to "English" and "physics" by the two groups of pupils, subtracted in the order (chosen subject-rejected subject), on the three factor traits or dimensions. The results are shown in Table 2.

Table 2 Mean Factor Score Differences for (Chosen Subject-Rejected Subject)

	Wise- foolish dimension	Masculine- feminine dimension	Hot- cold dimension
A group	78†	-73†	92†
S group	25*	75†	09

Decimals and zeroes omitted.

* Significant at 5%, † significant at 1%.

The two main features of the table are very clear. The A group differentiates sharply between the chosen subject and the rejected one in each of the three dimensions, while the S group differentiates as sharply only along the masculine-feminine dimension. Further, the S group differentiation along this latter dimension is in exactly the opposite direction to that given by the A group.

Osgood and his co-authors have suggested that the distance between any two nouns in the three dimensional semantic space defined by the factor score axes is a measure of the difference of meaning between the two nouns¹⁰. The distances between "English" and "physics" and the other nouns included in the survey were evaluated by finding the root mean square differences between the three factor scores given to each noun, and the A pupils were found to place "English" close to "home" ($d=0.61$), "success" ($d=0.81$), "good schoolmaster" ($d=0.83$), and "father" ($d=0.96$), and relatively far away from "games" ($d=1.35$), "rules" ($d=1.38$) and "physics" ($d=1.41$). "Physics" was placed close to "rules" ($d=0.17$), "work" ($d=0.75$), and "boy" ($d=1.12$), and far from "father" ($d=1.84$), "home" ($d=2.00$) and "pleasure" ($d=$

2.34). The S pupils placed "English" close to "physics" ($d=0.79$), "work" ($d=0.82$), "rules" ($d=0.83$) and "home" ($d=0.93$), and moderately far from "games" ($d=1.46$), "pleasure" ($d=1.42$), "good schoolmaster" ($d=1.53$) and "father" ($d=1.53$). "Physics" was placed close to "work" ($d=0.24$), "boy" ($d=0.71$), and "success" ($d=0.74$), and far from "good schoolmaster" ($d=1.11$), "home" ($d=1.14$) and "pleasure" ($d=1.61$).

It is clear that the S group pupils do not differentiate nearly as sharply as their A group counterparts between school subjects (except on the masculine-feminine factor of Table 2). The elements of the "home", "good", "schoolmaster" and "father" are missing from their chosen subjects, and they even opt for a course which they rate at a great distance from "pleasure". Conversely, the A group pupils select a course which contains a strong flavour of the feminine "home" and "pleasure" concept found by other workers in this field^{13,14}. It could be pertinent to recall that, at the time these results were obtained, the adolescent trend towards unisex was strongly under way. The breaking down of the distinctions between the masculine and the feminine, and the desire to avoid being labelled as "arts" or "science" (more than 30 per cent of our population now study mixed arts and science courses to A level), seem in retrospect to have been concomitant phenomena.

Yours faithfully,

S. W. HOCKEY

Marlborough College,
Wiltshire

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UNISIST

SIR,—While the leading article "Slowly but Steadily with Information" (*Nature*,

234, 268; 1971) is a fair summation of and comment on UNISIST, I feel that it does less than justice to the problems of exchanging information and current awareness and of copyright.

One of the most prevalent fallacies is that the average worker in basic research (whether in university, government, or industry) can keep up with the state-of-the-art by the means mentioned in the article. A few research workers can, those in relatively restricted field, those who are leaders in their field, and possibly some in the academic sphere. However, most research workers cannot, particularly those who are engaged in multidisciplinary research (for example, ecology) and those in government and industry.

Therefore, for the majority of people engaged in scientific research the most important part of the information exchange process is to, somehow, sort out from the great mass of published and quasi-published literature that which is relevant to their needs. All this must be done with the minimum of effort on the user's part, so that he is able to put the maximum effort into "reading and puzzling out what the other fellow means", which has been rightly identified as another important part of the information exchange process. This is, of course, why mechanized systems for retrospective and current awareness searching of the world's literature are so important and command so much attention at meetings like UNISIST.

To downgrade the importance of these systems, particularly on a world-wide basis, by assuming that they are not of primary importance to the research worker, is a significant error of judgment.

What appears to have been missed about copyright is that the development of new technology (for example, photocopying) has made the various copyright laws un-enforceable in any practical sense. Therefore, however sympathetic one may be to the concept of copyright and the views of the leader writer, it is essential to realize that the laws of copyright must be re-cast in the light not only of the present but of the future. Any other view is a denial of common-sense.

Yours faithfully,

R. M. McMULLEN

Information Retrieval Services,
100 Metcalfe Street,
Ottawa, Ontario,
K1A 0C8

Population Control

SIR,—In your leader "The Duke and ZPG" (*Nature*, 234, 499; 1971) you criticize the view that the British popula-

tion is growing too large, yet you make no attempt to examine the question "How large is too large?". It undoubtedly is true that it is much harder than it used to be for people to enjoy the beaches in summer; city streets are certainly more crowded; and the pressure of industry on the environment is obvious to all. Perhaps it is time the problem of the

optimal size of Britain's population was examined.

Although the birth rate has fallen since 1966, you admit that this is likely to be reversed in the next few years. The fact that a large part of our increased population is due to increased longevity (rather than a high birth rate) does not lessen the impact of the greater numbers. It is

irresponsible to preach complacency about population growth and to ridicule those who try to suggest remedies.

Yours faithfully,

J. M. IOANNOU

4 Regent Terrace,
Chapel Allerton,
Leeds LS7 4QL

Obituary

Professor J. D. Bernal



Photo: Henry Grant AIIP

THE recent death of J. D. Bernal, after a long and tragic illness, has robbed British science of one of its most outstanding and controversial figures.

John Desmond Bernal was born seventy years ago in Nenagh, Ireland, the eldest of four children. His father was a Catholic gentleman farmer; his mother a university educated American expatriate and a Protestant. Bernal's background was further variegated by his attendance at English public schools. Partly and paradoxically as the result of this mixture of national and religious traditions, he became a passionate adherent of both Roman Catholicism and Irish nationalism. It was also during this period that Bernal found himself attracted to mathematics and the physical sciences.

His decision to specialize in X-ray crystallography was made during his undergraduate years at Cambridge, so he joined the group of young and brilliant crystallographers that Sir William Bragg had brought together at the Royal Institution. Here, under the general guidance of Bragg himself, and with such workers as Kathleen Lonsdale and W. T. Astbury, he learned the techniques of X-ray crystallography and in 1924 he achieved his first success,

using them to determine the structure of graphite. He was in some ways a poor experimentalist, being impatient in a field that required long periods of concentration and accurate measurement. The instrument which was then almost universally employed in British X-ray crystallography, the ionization spectrometer, was slow and tedious, although very accurate, and very early in his experimental career Bernal decided that this method was not for him. This led him to search for simpler, less painstaking methods, which resulted in 1926 in the publication of his first paper of major importance—on the technique of single crystal rotation photography. This paper, which included charts for indexing rotation photographs, made these methods widely available to an English speaking audience for the first time.

In 1927 he returned to Cambridge to a lectureship in crystallography, and it was here that he first began to attract his own scientific followers—Dorothy Hodgkin, I. Fankuchen, M. F. Perutz, and many others. Although he worked on a wide range of substances, in part through contact with the Biochemistry Department he early became interested in biological molecules. Thus, in the thirties, a period of intense political activity, he at the same time did much of his most important scientific work, starting with the sterols, turning to crystalline proteins, and going on to viruses.

In 1932, during a study of the sterols, he was able to demonstrate that the conventional chemical formula for one of these compounds was incorrect, by showing that the size of the molecule from its chemical formula could not possibly fit into the unit cell, the dimensions of which he determined by crystallographic means.

In 1934 he and Crowfoot published the results of work on the crystalline protein, pepsin. Up until this time X-ray work on the crystalline proteins had been held up by the fact that, despite the apparently suitable nature of the crystals, the diffraction effects were in fact highly diffuse, and gave little or no evidence of a highly organized or regular molecular architecture. A number of crystallographers

had worked on proteins, but with the exception of fibre workers such as Astbury, little advance had been made. Bernal hit upon the simple expedient of taking pictures of wet rather than dry crystals, and he found that the resultant X-ray photographs included detail down to the atomic level. It was immediately clear that all the necessary detail was present for a full structure determination, if only it could be interpreted.

This work on pepsin, then, laid the foundations for modern protein crystallography, and it posed the question—how can the detail revealed by the photographs be interpreted? The problem was one well known to all crystallographers—the phase problem—although made more difficult by the size of the protein molecules. Much of Bernal's later work involved attempts to overcome the phase problem, and although in the end he was ultimately unsuccessful, he offered his co-workers some valuable hints. Thus, in 1939, he suggested two possible approaches, one of which, the isomorphous replacement method, was that successfully employed by Perutz and Kendrew in their work on haemoglobin and myoglobin. Again, he was one of the few crystallographers who really appreciated at an early stage that advanced methods of computing would be needed to process the volume of data involved in protein structure determination, and after the war he organized a research project on automatic methods of calculation.

In 1937 he moved to become Professor of Physics at Birkbeck College, London, and while continuing his protein work he also collaborated with Fankuchen in pioneering work on virus structure and the properties of viruses in solution. His work in pure science was interrupted by the outbreak of war, although he still maintained a lively interest in all crystallographic and biological work.

In post-war years Bernal did much less experimental scientific work himself. This was partly as a result of his wartime administrative experience, and partly because his interests, always wide ranging, were leading him into more general and speculative areas. Thus, while he organized a group at Birkbeck

to work on proteins, other X-ray work was carried out on a variety of practical problems, the structure of fuel ash, and the hardening of cement, for example. He developed his interest in water, using model building methods in an attempt to understand its structure. At the same time a major part of his energies now involved general biological problems as can be seen in at least two major books, *The Physical Basis of Life* (1950) and *The Origin of Life* (1967).

While Bernal did not follow up many of his best ideas, leaving this to others, none the less his own published scientific work was of absolutely major importance. This was recognized in the many scientific honours he received. He was elected a Fellow of the Royal Society in 1937, and in 1945 he was awarded the Royal Medal of the Royal Society. His high standing in the crystallographic community is reflected by the fact that he was President of the International Union of Crystallography from 1963 to 1966.

Bernal's self-definition as a scientist was exceptionally broad, because it explicitly encompassed ethical and political concerns. In 1923 he joined the Communist Party of Great Britain, with which he was closely associated throughout his life. The period of his most active involvement with politics dates, however, from the early thirties. From then until the outbreak of the Second World War, he helped spearhead a movement of young radical scientists through such organizations as the Cambridge Scientists' Anti-War Group and the Association of Scientific Workers. He was also a prominent participant in the early work of the British Association's Division for the Social and International Relations of Science (founded in 1938). Internationally, Bernal's friendships with socialist researchers in France and the

Soviet Union were instrumental in the foundation of the World Federation of Scientific Workers in 1946. As befitted the breadth of his intellectual interests, the "two cultures" phenomenon hardly affected Bernal, who numbered among his close acquaintances such non-scientists as Benjamin Farrington, Barbara Hepworth, Henry Moore and John Strachey.

Bernal was a thoroughgoing Marxist. His social philosophy, the product of a lifelong dialectic between his ideological beliefs and his professional experiences, was that of scientific socialism. From that vantage point—best summed up in *The Freedom of Necessity* (1949)—he boldly surveyed man's past in *Science in History* (3rd ed., 1965) and his possible future in *The World, the Flesh and the Devil* (1929). But the best-known of his works was *The Social Function of Science* (1939), a prophetic indictment of the non-use or mis-use of scientific resources in capitalist societies.

In an age of ceaseless warfare, Bernal was above all a partisan of peace. Not being a pacifist himself, his anti-war stance was subjected to the political vagaries of the Cold War. Bernal's attacks on militarized science in the West led to his removal from the Council of the British Association for the Advancement of Science in 1949. He incurred further enmity for his stand on biological warfare during the Korean War. But he will probably best be remembered for his crucial research on the physics of air raids between 1939 and 1945. The value of his contribution to the Allied war effort was recognized in his appointment as a personal science adviser to Lord Mountbatten. Bernal's dedication to peace has since been commemorated in the establishment of the Bernal Peace Library.

Scientifically and politically, the goals

which Bernal set himself were often beyond his reach. Yet when we consider how far his aims transcended those of almost all his contemporaries, we cannot help but admire the audacity and nobility of his life.

Thirty years ago Bernal wrote of the seventeenth-century philosopher Comenius that

"Where he excelled was in having in his own person the knowledge and experience that existed elsewhere scattered in many minds; and in having a burning faith in the practicability of what he propounded. In essence Comenius' mission was a religious one. . . . For him toleration, peace and justice were far more necessary elements of true religion than exhortation or force; education was the means by which it should be spread."

That tribute can now be extended to Bernal himself.

Announcements

University News

Dr W. G. Chaloner, University College London, has been appointed to the chair of botany tenable at Birkbeck College, University of London.

Mr P. S. Byrne has been appointed professor of general practice in the University of Manchester, and **Mr F. A. Langley** has been appointed to a personal chair in obstetrical and gynaecological pathology.

Dr E. M. Symonds, University of Adelaide, has been appointed to the foundation chair of obstetrics and gynaecology in the Medical School of the University of Nottingham.

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